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(54) **COMPOSITIONS AND METHODS FOR THE TREATMENT OF TUMOR OF HEMATOPOIETIC ORIGIN**

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(58) **Field of Classification Search**

None
See application file for complete search history.

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(57) **ABSTRACT**

The present invention is directed to compositions of matter useful for the treatment of hematopoietic tumor in mammals and to methods of using those compositions of matter for the same.

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(56)

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U.S. Appl. No. 14/181,529, filed May 13, 2014, Chen et al.

* cited by examiner

FIGURE 1

DNA105250

AGTGTGATGGATATCTGCAGAATTCGCCCTTATGGCGTTTGACGTCAGCTGCTTCTTTTG
GGTGGTGCTGTTTTCTGCCGGCTGTAAAGTCATCACCTCCTGGGATCAGATGTGCATTGA
GAAAGAAGCCAACAAAACATATAACTGTGAAAATTTAGGTCTCAGTGAAATCCCTGACAC
TCTACCAAACAACAAGAAATTTTTGGAAATTCAGCTTTAATTTTTTGCCTACAATTCACAA
TAGAACCTTCAGCAGACTCATGAATCTTACCTTTTTGGATTTAACTAGGTGCCAGATTAA
CTGGATACATGAAGACACTTTTTCAAAGCCATCATCAATTAAGCACACTTGTGTTAACTGG
AAATCCCTTGATATTCATGGCAGAAACATCGCTTAATGGGCCCAAGTCACTGAAGCATCT
TTTTCTTAATCCAAACGGGAATATCCAATCTCGAGTTTATTCAGTGACAATCTGGAAAA
CTTGGAAAGCTTGTATCTTGAAGCAACCATATTTCCCTCCATTAAGTTCCCAAAGACTT
CCCAGCACGGAAATCTGAAAGTACTGGATTTTCAGAATAATGCTATACACTACATCTCTAG
AGAAGACATGAGGTCTCTGGAGCAGGCCATCAACCTAAGCCTGAAGTTCAATGGCAATAA
TGTTAAAGGTATTGAGCTTGGGGCTTTTTGATTCAACGGTCTTCCAAAGTTTGAACTTGG
AGGAACTCCAAATTTGTCTGTATATTCAATGGTCTGCAGAACTCTACTACTCAGTCTCT
CTGGCTGGGAACATTTGAGGACATTGATGACGAAGATATTAGTTCAGCCATGCTCAAGGG
ACTCTGTGAAATGTCTGTGAGAGCCTCAACCTGCAGGAACACCGCTTCTCTGACATCTC
ATCCACCACATTTAGTGTCTCACCCAACTCCAAGAATGGATCTGACAGCAACTCACTT
GAAAGGGTTACCCTCTGGGATGAAGGGTCTGAACTTGCTCAAGAAATAGTTCTCAGTGT
AAATCATTTGATCAATTTGTGTCAAATCAGTGTGCCAATTTCCCTCCCTTACACACCT
CTACATCAGAGGCAACGTGAAGAACTTCACCTTGGTGTGGCTGCTGGAGAAACTAGG
AAACCTTCAGACACTTGATTTAAGCCATAATGACATAGAGGCTTCTGACTGCTGCAGTCT
GCAACTCAAAAACCTGTCCCACTTGCAAACCTTAAACCTGAGCCACAATGAGCCTCTTGG
TCTCCAGAGTCAGGCATTCAAAGAATGTCCTCAGCTAGAACTCCTCGATTTGGCATTTAC
CCGCTTACACATTAATGCTCCACAAGTCCCTTCCAAAACCTCCATTTCCCTCAGGTTCT
GAATCTCACTTACTGCTTCCCTTGATACCAGCAATCAGCATCTTCTAGCAGGCCTACCAGT
TCTCCGGCATCTCAACTTAAAAGGGAACTCACTTTCAAGATGGGACTATCACGAAGACCAA
CCTACTTCAGACCGTGGGCAGCTTGGAGGTTCTGATTTTGTCTCTTGTGGTCTCCTCTC
TATAGACCAGCAAGCATTCCACAGCTTGGGAAAAATGAGCCATGTAGACTTAAGCCACAA
CAGCCTGACATGCGACAGCATTGATTCTCTTAGCCATCTTAAGGGAACTACCTCAATCT
GGCTGCCAACAGCATTAAACATCATCTCACCCGTCCTCCCTATCTTGTCCCAGCAGAG
CACCATTAATTTAAGTCATAACCCCTGGACTGCACCTTGTGCGAATATTCATTTCTTAAC
ATGGTACAAAGAAAACCTGCACAACTTGAAGGCTCGGAGGAGACCAGTGTGCAAAACC
GCCATCTTAAGGGGAGTTAAGCTATCTGATGTCAAGCTTTCCCTGTGGGATTACAGCCAT
AGGCATTTCTTTCTCATAGTATTTCTATTATTGTTGGCTATTCTGCTATTTTTTTCAGT
TAAATACCTTCTCAGGTGGAAATACCAACACATTAGTGTGAAGGTTTCCAGAGAA

FIGURE 2A

DNA105250

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA105250

><subunit 1 of 1, 661 aa, 1 stop

><MW: 74165, 'pI: 6.34, NX(S/T): 11

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SFNFLTPIHNRFTFSRLMNLTFDLTRCQINWIHEDTFQSHHQLSTLVLTGNPLIFMAETS
LNGPKSLKHLFLIQTGISNLEFIPVHNLENLESYLGSNHISSIKFKDFPARNLKVLDL
QNNAIHYISREDMRSLEQAINLSLNFNGNNVKGIELGAFDSTVVFQSLNFGGTPNLSVIFN
GLQNSTTQSLWLGTFEDIDDEDISSAMKGLCEMSVESLNLQEHFRFSDISSTTFQCFTQL
QELDLTATHLKGLPSPGMKGLNLLKKLVLSVNHFDQLCQISAAFPPLTHLYIRGNVKKLH
LGVGCLEKLGNLQTL,DLSHNDIEASDCCSLQLKNLSHLQTLNLSHNEPLGLQSQAFCPC
QLELLDLAFTRLHINAPQSPFQNLHFLQVLNLTFCFLDTSNQHLLAGLPLVLRHLNKGNH
FQDGTITKTNLQTVGSLEVLILSSCGLLSIDQAFHSLGKMSHVLDLSHNSLTCDSIDSL
SHLKGIYLNLAANSINIISPRLLPILSQQSTINLSHNPLDCTCSNIHFLTWYKENLHKLE
GSEETTCANPPSLRGVKLSVVKLSCGITAIGIFFLIVFLLLLAILLFFAVKYLLRWKYQH
I

Signal sequence.

amino acids 1-18

Transmembrane domain.

amino acids 489-509, 628-648

Leucine Rich Repeat.

amino acids 54-77, 78-101, 102-125, 126-149, 150-171, 174-197, 275-298, 299-321, 322-348, 371-396, 397-420, 421-445, 446-469, 470-493, 497-520, 521-544

Leucine Rich Repeat C-terminal Domain.

amino acids 577-626

N-glycosylation site.

amino acids 34-37, 53-56, 70-73, 78-81, 201-204, 234-237, 244-247, 394-397, 401-405, 451-454, 573-576

Protein kinase C phosphorylation site.

amino acids 126-128, 163-165, 559-561, 612-614

Casein kinase II phosphorylation site.

amino acids 22-25, 80-83, 136-141, 189-192, 254-257, 378-381, 404-407, 523-526

N-myristoylation site.

amino acids 213-218, 217-222, 230-235, 241-246, 312-317, 370-375, 545-560, 601-606, 615-620

FIGURE 2B

**Prokaryotic membrane lipoprotein lipid attachment site.
amino acids 8-18**

**Leucine zipper pattern.
amino acids 44-65, 450-471**

FIGURE 3

DNA150004

CAGCAGTAGGCCTTGCCCTCAGATCCAAGGTCCTCGGAAGAGGCCATGTCTACCCTCAAT
GACACTCATGGAGGAAATGCTGAGAGAAGCATTGAGATGCATGACACAAGGTAAGACTGC
CAAAAATCTTGTCTCTGCTCTCCTCATTGTTGTTATTTGTTTTATTTTFFAGGAGTTTTGAG
AGCAAAATGACAACACCCAGAAATTCAGTAAATGGGACTTTCCCGGCAGAGCCAATGAAA
GGCCCTATTGCTATGCAATCTGGTCCAAAACCACTTTCAGGAGGATGTCTTCACTGGTG
GGCCCCACGCAAAGCTTCTTCATGAGGGAATCTAAGACTTTGGGGGCTGTCCAGATTATG
AATGGGCTCTTCCACATGCCCCGGGGGGTCTTCTGATGATCCCAGCAGGGATCTATGCA
CCCATCTGTGTGACTGTGTGGTACCCTCTCTGGGGAGGCATTATGTATATTATTTCCGGA
TCACTCCTGGCAGCAACGGAGAAAACTCCAGGAAGTGTGTTGGTCAAAGGAAAAATGATA
ATGAATTCATTGAGCCTCTTTGCTGCCATTTCTGGAATGATTCTTCAATCATGGACATA
CTTAATATATAAAATTTCCCATTTTTTAAAAATGGAGAGTCTGAATTTTATTAGAGCTCAC
ACACCATATATTAACATATACAACCTGTGAACCAGCTAATCCCTCTGAGAAAACTCCCA
TCTACCAATACTGTTACAGCATAACAATCTCTGTTCTTGGGCATTTTGTGATGATGCTG
ATCTTTGCCCTTCTTCCAGGAACCTGTAATAGCTGGCATCGTTGAGAATGAATGGAAAAGA
ACGTGCTCCAGACCCAAATCTAACATAGTTCTCCTGTGACAGAGAAAAAAGAACAG
ACTATTGAAATAAAAGAAGAAGTGGTGGGCTAACTGAAACATCTTCCCAACCAAAGAAAT
GAAGAAGACATTGAAATATTCCAATCCAAGAAGAGGAAGAAGAAGAAACAGAGACGAAC
TTTCCAGAACCTCCCAAGATCAGGAATCCTCACCAATAGAAAATGACAGCTCTCCTTAA
GTGATTTCTTCTGTTTTCTGTTTCTTTTTTAAACATTAGTGTTCATAGCTTCCAAGAGA
CATGCTGACTTTTCATTTCTTGGAGTACTCTGCACATACGCACCACATCTCTATCTGGCCT
TTGCATGGAGTGACCATAGCTCCTTCTCTTACATTGAATGTAGAGAATGTAGCCATTG
TAGCAGCTTGTGTTGTACGCTTCTTCTTTGAGCAACTTTCTTACACTGAAGAAAGGCA
GAATGAGTGCTTCAGAATGTGATTTCCCTACTAACCTGTTTCTTGGATAGGCTTTTTAGTA
TAGTATTTTTTTTTGTCATTTTTCTCCATCAACAACCAGGGAGACTGCACCTGATGGAAAA
GATATATGACTGCTTCATGACATTCCTAAACTATCTTTTTTTTTATTTCCACATCTACGTTT
TTGGTGGAGTCCCTTTTGCATCATTGTTTTAAGGATGATAAAAAAATAACAACCTAGGG
ACAATACAGAACCCATTCCATTTATCTTTCTACAGGGCTGACATTTGTGGCACATTTCTAG
AGTTACCACACCCCATGAGGGAAGCTCTAAATAGCCAACCCCATCTGTTTTTTGTAAAA
ACAGCATAGCTTATACATGGACATGTCTCTGCTTAACTTTTCTAACTCCCCTCTAGG
CTATTGTTTGCATGTCTACCTACTTTTAGCCATTATGCGAGAAAAGAAAAAATGACCAT
AGAAAATGCCACCATGAGGTGCCAAAATTTCAAATAATAATTAACATTTAGTTATATTTA
TAATTTCCAGATGACAAAGTATTTTCATCAAATAACTTCATTTGATGTTCCATGATCAAGA
AAGAAATCCCTATCTCTATTTTACAAGTAATTCAAAGAGGCCAAAATAACTTGTAAACAAGA
AAAGGTAACCTGTCAACAGTCATAACTAGTAATTATGAGAGCCTTGTTTTATAACCAGGT
CTTCTTACTCAAATCCTGTGATGTTTGAATAACCAAATTTGCTCTCCAATGTCTGCATA
AATGTGAGAGCCAAGTCAACAGCTTTTATCAAGAATTTACTCTCTGACCAGCAATAAAC
AAGCACTGAGAGACACAGAGAGCCAGATTCAGATTTTACCCATGGGGATAAAAAGACTCA
GACTTTACCCACATTTGGAAAACCTACTTGCATCATAAATATAATAAAGTGGTAGTTTAT
ATGAAGCAGACACTAAGTGTCTATAGACACTCTCAGAATATCATACTTGGAAACAATGTAA
TTAAAATGCCGAATCTGAGTCAACAGCTGCCCTACTTTTCAATTCAGATATACTAGTACC
TTACCTAGAAAATAATGTTAACCTAGGGTGAAGTCACTATAATCTGTAGTCTATTATTTGG
GCATTTGCTACATGATGAGTGTGCCAGATTGTGGCAGGTAAGAGACAATGTAATTTGC
ACTCCCTATGATATTTCTACATTTTGTAGCGACCCTAGTGGAGACATTTCCCAAAATTA
GAAAAAAGGAGATAGAAGATTTCTGTCTATGTAAAGTTCTCAAATTTGTTCTAAATTA
ATAAACTATCTTTGTGTTCA

FIGURE 4

DNA150004

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA150004
><subunit 1 of 1, 297 aa, 1 stop
><MW: 33077, pI: 5.10, NX(S/T): 3
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MTTPRNSVNGTFFPAEPMKGP IAMQSGPKPLFRMSSLVGPTQSFFMRESKTLGAVQIMNG
LFHIALGGLLMIPAGIYAPICVTVWYPLWGGIMYIISGSLLAATEKNSRKCLVKGKMIMN
SLSLFAAISGMILSIMDILNIKISHFLKMESLNFIRAHTPYINIYNCEPANPSEKNSPST
QYCYSIQSLFLGILSVMLIFAFFQELVIAGIVENEWKRTCSRPKSNIVLLSABEKKEQTI
EIKEEVVGLTETSSQPKNEEDIEIPIQEEEEETETNFPEPPQDQESSPIENDSSP
```

Transmembrane domain.

amino acids 56-76, 82-102, 118-138, 187-207

CD 20/IgE Fc Receptor Beta Subunit Family.

amino acids 58-224.

N-glycosylation site.

amino acids 9-12, 293-296

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 32-35

Protein kinase C phosphorylation site.

amino acids 3-5, 104-106, 108-110, 173-175

Casein kinase II phosphorylation site.

amino acids 134-137, 231-234, 289-292

N-myristoylation site.

amino acids 10-15, 98-103, 130-135, 210-215, 248-253

FIGURE 5

DNA 182432

GTGGGTGACCAAGAGTACATCTCTTTTCAAATAGCTGGATTAGGTCCTC ATGCTGCTGTG
GTCATTGCTGGTCATCTTTGATGCAGTCACTGAACAGGCAGATTGCTGACCCTTGTGGC
GCCCTCTCTGTCTTTCGAAGGAGACAGCATCGTTCTGAAATGCCAGGGAGAACAGAAGT
GAAAATTCAGAAGATGGCTTACCATAAGGATAACAAAGAGTTATCTGTTTTCAAAAATT
CTCAGATTTCCCTTATCCAAAGTGCAGTTTAAAGTGACAGTGGTAACTATTTCTGTAGTAC
CAAAGGACAACCTCTTTCTCTGGGATAAACTTCAAATATAGTAAAGATAAAAAGTCCAAGA
GCTCTTTCAACGTCCGTGTGCTGACTGCCAGCTCCTCCAGCCCATCGAAGGGGGTCCAGT
GAGCCTGAAATGTGAGACCCGGCTCTCTCCACAGAGGTTGGATGTTCAACTCCAGTTCTG
CTTCTTCAGAGAAAACCAGGTCCTGGGGTCAGGCTGGAGCAGCTCTCCGGAGCTCCAGAT
TTCTGCCGTGTGGAGTGAAGACACAGGCTTACTGGTGCAAGGCAGAAACGGTGACTCA
CAGGATCAGAAAACAGAGCCTCCAATCCAGATTACGTGCAGAGAATCCCCATCTCTAA
TGTAAGCTTGGAGATCCGGGCCCGGGGACAGGTGACTGAAGGACAAAACCTGATCCT
GCTCTGCTCAGTGGCTGGGGGTACAGGAAATGTCACATTCTCCTGGTACAGAGAGGCCAC
AGGAACCAGTATGGGAAAGAAAACCCAGCGTTCCCTGTGAGCAGAGCTGGAGATCCAGC
TGTGAAAGAGAGTGTGCGGCAAATATTACTGTAGAGCTGACAACGGCCATGTGCCTAT
CCAGAGCAAGGTGGTGAATATCCCTGTGAGAATTCCAGTGTCTCGCCCTGTCTCACCCCT
CAGGTCCTCGGGGCCAGGCTGCAGTGGGGACCTGCTGGAGCTTCACTGTGAGGCCCT
GAGAGGCTCTCCCCAATCTTGTACCAATTTTATCATGAGGATGTCACCCTTGGGAACAG
CTCGGCCCCCTCTGGAGGAGGGCCCTCTTCAACCTCTCTTTGACTGCAGAACATTTCTGG
AACTACTCCTGTGAGGCCAACAACGSCCTGGGGGCCAGTGCAGTGAAGCAGTGCCAGT
CTCCATCTCAGGACCTGATGGCTATAGAAGAGACCTCATGACAGCTGGAGTTCTCTGGGG
ACTGTTTGGTGTCTTGGTTTCACTGCTGTTGCTTTGCTGTTGTATGCCTTGTTCACAA
GATATCAGGAGAAAAGTTCTGCCACTAATGAACCCAGAGGGCTTCCAGGCCAAATCCTCA
AGAGTTCACCTATTCAAGCCCAACCCAGACATGGAGGAGCTGCAGCCAGTGTATGTCAA
TGTGGGCTCTGTAGATGTGGATGTGGTTTATTTCTCAGGCTGGAGCATGCAGCAGCCAGA
AAGCTCAGCAAACATCAGGACACTTCTGGAGAACAAGGACTCCCAAGTCATCTACTCTTC
TGTGAAGAAATCATAACACTTGGAGGAATCAGAAGGGAAGATCAACAGCAAGGATGGGGC
ATCATTAAGACTTGTATAAAACCTTATGAAAATGCTTGAGGCTTATCACCTGCCACAGC
CAGAACGTGCCTCAGGAGGCACCTCCTGTCAATTTTGTCTGATGATGTTTCTTCTCAA
TATCTCTTTTACCTATCAATATTCATTGAACCTGCTGCTACATCCAGACACTGTGCAAA
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FIGURE 6A

DNA 182432

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><subunit 1 of 1, 508 aa, 1 stop

><MW: 55542, pI: 6.30, NX(S/T): 5

MLLWSLLVIFDAVTEQADSLTLVAPSSVFEGDSIVLKCQGEQNWKIQKMAYHKDNKELSV
FKKFSDFLIQSAVLSDSGNYFCSTKQQLFLWDKTSNIVKIKVQELFQRPVLTASSFQPIE
GGPVSLKCETRLSPQRLDVQLQFCFFRENQVLGSGWSSPELQISAVWSEDTGSYWCKAE
TVTHRIRKQSLQSQIHVQRIPISNVSLEIRAPGGQVTEGQKLILLCSVAGGTGNVTFWSY
REATGTSMGKKTQRSLTABLEIPAVKESDAGKYICRADNGHVPIQSKVVNIPVRI PVS RP
VLTLRSPGAQA AVGD LLELHCEALRGSPPILYQFYHEDVTLGNSSAPSGGGASFNL SLTA
EHSGNYSCEANGLGAQCSEAVPVVISGPDGYRRDLMTAGVLWGLFGVLGFTGVALLLYA
LFHKISGESSATNEPRGASRPNPQEFTYSSPTPDMEELQPVYVNVGSDVDV VVYSQVWSM
QQPESSANIRTLLENKDSQVIYSSVKKS

Signal sequence.

amino acids 1-14.

Transmembrane domain.

amino acids 400-420.

Immunoglobulin domain.

amino acids 17-84, 121-179, 219-277, 314-370.

N-glycosylation site.

amino acids 204-207, 234-237, 343-346, 355-358, 365-368

Glycosaminoglycan attachment site.

amino acids 348-351

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 62-65, 187-190

Protein kinase C phosphorylation site.

amino acids 83-85, 125-127, 183-185, 252-254, 303-305, 504-506

Casein kinase II phosphorylation site.

amino acids 27-30, 158-161, 387-390, 491-494

Tyrosine kinase phosphorylation site.

amino acids 266-273

N-myristoylation site.

amino acids 78-83, 121-126, 153-158, 173-178, 213-218, 230-235, 245-250, 308-313, 349-354, 351-356, 364-369, 375-360, 400-405

FIGURE 6B

**Amidation site.
amino acids 248-251**

FIGURE 7

DNA225785

TGCTGCAACTCAAAC TAACCAACCCACTGGGAGAAG ATGCCTGGGGGTCCAGGAGTCCTC
CAAGCTCTGCCTGCCACCATCTTCCTCCTCTTCCTGCTGTCTGCTGTCTACCTGGGCCCT
GGGTGCCAGGCCCTGTGGATGCACAAGGTCCCAGCATATTGATGGTGAGCCTGGGGGAA
GACGCCCACTTCCAATGCCCGCACAATAGCAGCAACAACGCCAACGTCACCTGGTGGCGC
GTCCTCCATGGCAACTACACGTGGCCCCCTGAGTTCTTGGGCCCGGGCGAGGACCCCAAT
GGTACGCTGATCATCCAGAATGTGAACAAGAGCCATGGGGGCATATACGTGTGCCGGGTC
CAGGAGGGCAACGAGTCATAACAGCAGTCCTGCCGCACCTACCTCCGCGTGCGCCAGCCG
CCCCCAGGCCCTTCTTGGACATGGGGGAGGGCACCAGAACC GAATCATCACAGCCGAG
GGGATCATCCTCCTGTCTGCGCGGTGGTGCCTGGGACGCTGCTGCTGTTT CAGGAAACGA
TGGCAGAACGAGAAGCTCGGGTTGGATGCCGGGATGAATATGAAGATGAAAACCTTTAT
GAAGGCCTGAACCTGGACGACTGCTCCATGTATGAGGACATCTCCGGGGCCTCCAGGGC
ACCTACCAGGATGTGGCAGCCTCAACATAGGAGATGTCCAGCTGGAGAAGCCG TGACCAC
CCCTACTCCTGCCAGGCTGCCCCCGCTGCTGTGCACCCAGCTCCAGTGTCTCAGCTCAC
TTCCCTGGGACATTCTCCTTT CAGCCCTTCTGGGGCTTCTTAGTCATAITCCCCCAGT
GGGGGTGGGAGGGTAACCTCACTCTTCTCCAGGCCAGGCCTCCTTGGACTCCCCTGGGG
GTGTCCCACTCTTCTCCTCTAAACTGCCCCACCTCCTAACCTAATCCCCAGCCCCGC
TGCCTTTCCAGGCTCCCCTCAGCCAGCGGGTAATGAGCCCTTAATCGCTGCCTCTAGGG
GAGCTGATTGTAGCAGCCTCGTTAGTGTACCCCCCTCCTCCCTGATCTGTCAGGGCCACT
TAGTGATAATAAATTCCTTCCCAACTGC

FIGURE 8

DNA225785

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA225785

><subunit 1 of 1, 226 aa, 1 stop

><MW: 25038, pI: 4.91, NX(S/T): 6

MPGGPGVQLQALPATIFLLELLSAVYLGPGCOALWMHKVPASLMVSLGEDAHFQCPHNSSN
NANVTWWRVHLHGNYTWPPEFLGPGEDPNGTLIIQNVNKS HGGIYVCRVQEGNESYQQSCG
TYLRVRQPPRPFLDMGEGTKNRITAEGLILLFCAVVPGTLLLFRKRWQNEKLGLDAGD
EYEDENLYEGLNLDDCSMYEDISRGLQGTYQDVGSLNIGDVQLEKP

Signal sequence.

amino acids 1-29.

Transmembrane domain.

amino acids 143-163.

Immunoreceptor tyrosine-based activation motif.

amino acids 185-205.

N-glycosylation site.

amino acids 57-60, 63-66, 73-76, 88-91, 97-100, 112-115

Casein kinase II phosphorylation site.

amino acids 45-48, 197-200, 209-212.

N-myristoylation site.

amino acids 6-11, 102-107, 175-180, 205-210.

Ribosomal protein S2 signature 1.

amino acids 16-27.

FIGURE 9

DNA225786

CAGGGGACAGGCTGCAGCCGGTGCAGTTACACGTTTTCTCCAAGGAGCCTCGGACGTTG
TCACGGGTTTGGGGTCGGGGACAGAGCAGTGACCATGGCCAGGCTGGCGTTGTCTCCTGT
GCCAGCCACTGGATGGTGGCGTTGCTGCTGCTCTCAGCTGAGCCAGTACCAGCAGC
CAGATCGGAGGACCGGTACCGGAATCCCAAAGGTAGTGCTTGTTCGCGGATCTGGCAGAG
CCCACGTTTCATAGCCAGGAAACGGGGCTTCACGGTGAAAATGCACTGCTACATGAACAG
CGCCTCCGGCAATGTGAGCTGGCTCTGGAAGCAGGAGATGGACGAGAATCCCAGCAGCT
GAAGCTGGAAAAGGGCCGCATGGAAGAGTCCCAGAACGAATCTCTCGCCACCCTCACCAT
CCAAGGCATCCGGTTTGAGGACAATGGCATCTACTTCTGTCAGCAGAAGTGCAACAACAC
CTCGGAGGTCTACCAGGGCTGCGGCACAGAGCTGCGAGTCATGGGATTCAGCACCTTGGC
ACAGCTGAAGCAGAGGAACACGCTGAAGGATGGTATCATCATGATCCAGACGCTGCTGAT
CATCCTCTTCATCATCGTGCTATCTTCTCTGCTGCTGGACAAGGATGACAGCAAGGCTGG
CATGGAGGAAGATCACACCTACGAGGGCCTGGACATTGACCAGACAGCCACCTATGAGGA
CATAGTGACGCTGCGGACAGGGGAAGTGAAGTGGTCTGTAGGTGAGCACCCAGGCCAGGA
GTGAGAGCCAGGTCGCCCCATGACCTGGGTGCAGGCTCCCTGGCCTCAGTGA CTGCTCG
GAGCTGCCCTGGCTCATGGCCCAACCCCTTCTCTGGACCCCCAGCTGGCCTCTGAAGCTG
GCCACCAGAGCTGCCATTTGTCTCCAGCCCTGGTCCCCAGCTCTTGCCAAAGGGCCTG
GAGTAGAAGGACAACAGGGCAGCAACTTGGAGGGAGTTCTCTGGGGATGGACGGGACCCA
GCCTTCTGGGGGTGCTATGAGGTGATCCGTCCCCACACATGGGATGGGGAGGCAGAGAC
TGGTCCAGAGCCCGCAAATGGACTCGGAGCCGAGGGCTCCAGCAGAGCTTGGGAAGGG
CCATGGACCCAACTGGGCCCCAGAAGAGCCACAGGAACATCATTCCTCTCCCGCAACCAC
TCCCACCCAGGGAGGCCCTGGCCTCCAGTGCCCTCCCCCGTGAATAAACGGTGTGTCC
TGAGAAACCA

FIGURE 10

DNA225786

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA225786

><subunit 1 of 1, 229 aa, 1 stop

><MW: 26048, pI: 5.86, NX(S/T): 4

MARLALSPVPSHWMVALLLLLLSAEPVPAARSEDYRNPKGSACSRIWQSPRFIARKRGFT
VXMHCYMNSASGNVSWLWKQEMDENPQQLKLEKGRMEESQNESLATLTIQGIRFEDNGIY
FCQQKCNNTSEVYQCGTELRVMGFSTLAQLKQRNTLKDGIIMIQTLLIILFIIIVPIFL
LDKDDSKAGMEEDHTYEGLDIDQTATYEDIVTLRTGEVKWSVGEHPGQE

Signal sequence.

amino acids 1-28.

Transmembrane domain.

amino acids 5-25, 159-179.

Immunoglobulin domain.

amino acids 58-124.

Immunoreceptor tyrosine-based activation motif.

amino acids 193-213.

N-glycosylation site.

amino acids 73-76, 101-104, 127-130, 128-131.

Protein kinase C phosphorylation site.

amino acids 49-51, 60-62, 156-158, 212-214.

Casein kinase II phosphorylation site.

amino acids 99-102, 156-159, 206-209, 221-224.

Tyrosine kinase phosphorylation site.

amino acids 113-120.

N-myristoylation site.

amino acids 40-45, 118-123.

FIGURE 11A

DNA225875

GCCCTCCAGAGCTGCCGGACGCTCGCGGGTCTCGGAACGCATCCCGCCGCGGGGGCTTC
GGCCGTGGCATGGGCGCCGCGGGCCTGCTCGGGGTTTTCTTGGCTCTCGTCCGACCGGGG
GTCTCGGGATTTCTTGTGGCTCTCCTCCGCCTATCCTAAATGGCCGGATTAGTTATTAT
TCTACCCCCATTGCTGTTGGTACCCTGATAAGGTACAGTTGTTTCAGGTACCTTCCGCCTC
ATTGAGAAAAAAGTCTATTATGCATAACTAAAGACAAAGTGGATGGAACCTGGGATAAA
CCTGCTCCTAAATGTGAATATTTCAATAAATATTTCTTGGCCCTGAGCCCATAGTACCA
GGAGGATACAAAATTAGAGGCTCTACACCCTACAGACATGGTGATTCTGTGACATTTGCC
TGTA~~AAA~~ACCAACTTCTCCATGAACGGAAACAAGTCTGTTTGGTGTCAAGCAAATAATATG
TGGGGCCGACACGACTACCAACCTGTGTAAGTGT~~TTT~~CCCTCTCGAGTGTCCAGCACTT
CCTATGATCCACAATGGACATCACACAAGTGAGAAATGTTGGCTCCATTGCTCCAGGATTG
TCTGTGACTTACAGCTGTGAATCTGGTTACTTGTCTGTTGGAGAAAAGATCATTAACTGT
TTGTCTTCGGGAAAAAGGAGTGTCTCCCCCACATGTGAAGAGGCACGCTGTAAATCT
CTAGGACGATTTCCCAATGGGAAGGTAAAGGAGCCTCCAATCTCCGGTGGTGTAACT
GCAA~~ACT~~TTTTCTGTGATGAAGGGTATCGACTGCAAGGCCACCTTCTAGTCGGTGTGTA
ATTGCTGGACAGGGAGTTGCTTGGACCAAATGCCAGTATGTGAAGAAATTTTGGCCA
TCACCTCCCCCTATTCTCAATGGGAAGACATATAGGCAACTCACTAGCAAATGTCTCATAT
GGAAGCATAGTCACTTACACTTGTGACCCGGACCCAGAGGAAGGAGTGA~~ACT~~TTCATCCTT
ATTGGAGAGAGCACTCTCCGTTGTACAGTTGATAGTCAGAAGACTGGGACCTGGAGTGGC
CCTGCCCCAGCTGTGA~~ACT~~TTTCTACTTCTGCGGTTCAAGTGTCCACATCCCCAGATCCTA
AGAGGCCGAATGGTATCTGGGCAGAAAAGATCGATATACCTATAACGACACTGTGATATTT
GCTTGCATGTTTTGGCTTCACTTGAAGGGCAGCAAGCAAATCCGATGCAATGCCCAAGGC
ACATGGGAGCCATCTGCACCAGTCTGTGAAAAGGAATGCCAGGCCCTCCTAACATCCTC
AATGGGCAAAAGGAAGATAGACACATGGTCCGCTTTGACCCGGAAACATCTATAAAATAT
AGCTGTAACCCTGGCTATGTGCTGGTGGGAGAAGAATCCATACAGTGTACCTCTGAGGGG
GTGTGGACACCCCTGTACCCCAATGCAAAGTGGCAGCGTGTGAAGCTACAGGAAGGCAA
CTCTTGACAAAACCCAGCACCAATTTGTTAGACCAGATGTCAACTCTTCTGTGGTGA
GGGTACAAGTTAAGTGGGAGTGT~~T~~TATCAGGAGTGTCAAGGCACAATTCCTTGGTTTTATG
GAGATTCTGCTTTGTAAAGAAATCACCTGCCACCACCCCTGTTATCTACAATGGGGCA
CACACCGGGAGTTCCTTAGAAGATTTTCCATATGGAACCAGGTCACCTACACATGTAAC
CCTGGGCCAGAAAAGAGGAGTGAATTCAGCCTCATTGGAGAGACCAATCCGTTGTACA
AGCAATGATCAAGAAAGAGGCACCTGGAGTGGCCCTGCTCCCCTATGTAAACTTTCCCTC
CTTGCTGTCCAGTCTCACATGTCCATATTGCAAATGGATACAAGATATCTGGCAAGGAA
GCCCCATATTTCTACAATGACACTGTGACATTCAGTGTATAGTGGATTTACTTTGAAG
GGCAGTAGTCAGATTCGTTGCAAAGCTGATAACACCTGGGATCCTGAAATACCAGTTTGT
GAAAAAGAAACATGCCAGCATGTGAGACAGAGTCTTCAAGAACTTCCAGCTGGTTCACGT
GTGGAGCTAGTTAATACGTCTGCCAAGATGGGTACCAGTTGACTGGACATGCTTATCAG
ATGTGTCAAGATGCTGAAAAAGGAATTTGGTTCAAAAAGATTCCACTTTGTAAAGTTATT
CACTGTCA~~CCCT~~CCACCAGTGATTGTCAATGGGAAGCACACAGGGATGATGGCAGAAAAC
TTTCTATATGGAATGAAGTCTCTTATGAATGTGACCAAGGATTCTATCTCCTGGGAGAG
AAAAAATGTCAGTGCAGAAGTGATTCTAAAGGACATGGATCTTGGAGCGGGCCTTCCCCA
CAGTGTACGATCTCCTCCTGTGACTCGCTGCCCTAATCCAGAAGTCAAACATGGGTAC
AAGCTCAATAAAAACACATTTCTGCATATTTCCACAATGCATAGTGTATGTTGACTGCAAT
CCTGGCTTCATCATGAATGGTAGTCCGCTGATTAGGTGTCATACCTGATAACACATGGGTG

FIGURE 11B

CCAGGTGTGCCAACTTGTATGAAAAAGCCTTCATAGGGTGTCCACCTCCGCCTAAGACC
CCTAACGGGAACCATACTGGTGGAACATAGCTCGATTTTCTCCTGGAATGTCAATCCTG
TACAGCTGTGACCAAGGCTACCTGCTGGTGGGAGAGGCACTCCTTCTTGCACACATGAG
GGAACCTGGAGCCAACCTGCCCTCATTTGTAAGAGGTAAACTGTAGCTCACCAGCAGAT
ATGGATGGAATCCAGAAAGGGCTGGAAACCAAGGAAAATGTATCAGTATGGAGCTGTTGTA
ACTCTGGAGTGTGAAGATGGGTATATGCTGGAAGGCAGTCCCCAGAGCCAGTGCCAAATCG
GATCACCAATGGAACCTCCCTGGCGGTTTGCAGATCCCGTTCCTTGCTCCTGTCCCTT
TGTGGTATGCTGTCAGGTTTGATACTTCTTACCTTCTTGATTGTCAATACCTTATACGTG
ATATCAAAACACAGAGAACGCAATTATTATACAGATACAAGCCAGAAAGAAGCTTTTCAT
TTAGAAGCACGAGAAGTATATTCTGTTGATCCATACAACCCAGCCAGC TGATCAGAAGAC
AAACTGGTGTGTCCTCATTTGCTTGGAAATCAGCGGAATATTGATTAGAAAGAACTGCT
CTAATATCAGCAAGTCTCTTATATGGCCTCAAGATCAATGAAATGATGTCATAAGCGAT
CACTTCTATATGCACTTATTCTCAAGAAGAACATCTTATGGTAAAGATGGGAGCCAG
TTTCACTGCCATATACTCTTCAAGGACTTCTGAAGCCTCACTTATGAGATGCCTGAAGC
CAGGCCATGGCTATAAACAATTACATGGCTCTAAAAAGTTTTGCCCCTTTTAAAGGAAGGC
ACTAAAAAGAGCTGTCCCTGGTATCTAGACCCATCTTCTTTTGAATCAGCATACTCAAT
GTTACTATCTGCTTTTGGTTATAATGTGTTTTTAATTATCTAAAGTATGAAGCATTTTCT
GGGTTATGATGGCCTTACCTTTATTAGGAAGTATGGTTTTATTTTGATAGTAGCTTCCT
CCTCTGGTGGTGTAAATCATTTTCAATTTTACCCTTACTGTTGAGTTTCTCTCACATTAC
TGTATATACTTTGCCCTTCCATAATCACTCAGTGATTGCAATTTGCACAAGTTTTTTTAA
ATTATGGGAATCAAGATTTAATCCTAGAGATTTGGTGTACAATTCAGGCTTTGGATGTTT
CTTTAGCAGTTTTGTGATAAGTTCTAGTTGCTTGTAATAATTCACTTAATAATGTGTACA
TTAGTCATTCATAAATTGTAATTGTAAGAAAA

FIGURE 12A

DNA225875

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA225875

><subunit 1 of 1, 1033 aa, 1 stop

><MW: 112992, pI: 7.78, NX(S/T): 11

MGAAGLLGVFLALVAPGVLGISCGSPPPILNGRISYYSTPIAVGTVIRVSCSGTFRLLIGE
KSLLCITKDKVDGTWDKPAKCEYFNKYSSCPEPIVPGGYKIRGSTPYRHGDSVTFACKT
NFSMNGNKSVMWCQANNMWGPTLPTCVSVFPLECPALPMIHNGHHTSENVGSIAPGLSVT
YSCESGYLLVGEKIINCLSSGKWSAVPPTCEEARCKSLGRFPNGKVKEPPILRVGVTANF
FCDEGYRLQGFPSSRCVIAQGVAWTKMPVCEEIFCPSPPPILNGRHIGNSLANVSYGSI
VTTYCDPDPEEGVNFILIGESTLRCVTDSQKTGTWSGPAFRCELSTSAVQCQPHQILRGR
MVSQKDRYTYNDTVIFACMFGFTLKGSKQIRCNAQGTWEPSAPVCEKECQAPPNINLNGQ
KEDRHMVRFDPGTSIKYSCNPGYVLVGEESIQTSEGVTWPPVPQCKVAACEATGRQLLT
KPOHQFVRPDVNSSCGEGYKLSGSVYQECQGTIPWFMEIRLCKEITCPPPPVIYNGAHTG
SSELEDFPYGTTVTYTCNPGPERGVEFSLIGESTIRCTSNDQERGTWSGPAFLCKLSLLAV
QCSHVHIANGYKISGKEAPYFYNDTVTFKCYSGFTLKGSSQIRCKADNTWDPEIPVCEKE
TCQHVRSQELPAGSRVELVNTSCQDGYQLTGHAYQMCQDAENGIWFKKIPLCKVIHCH
PPPVIYNGKHTGMMMAENFLYGNEVSYECDQGFYLLGEEKLQCRSDSKGHGWSGSPQCL
RSPPVTRCPNPEVKHGYKLNKTHSAYSHNDIVYVDCNPGFIMNGSRVIRCHTDNTWVPGV
PTCMKKAFIGCPPFPKTPNGNHTGGNIARFSPGMSILYSCDQGYLLVGEALLLCTHEGTW
SQPAPHCKEVCNCSPPADMDGIQKGLEPRKMYQYGAVVTLCEEDGYMLEGSPQSQCSDHQ
WNPPLAVCRSRSLAPVLCGIAAGLILLTFLIVITLYVISKHRERNYYTDTSQKEAFHLEA
REVYSVDPYNPAS

Signal sequence.

amino acids 1-20.

Transmembrane domain.

amino acids 973-993.

Sushi domain (SCR repeat).

amino acids 23-82, 91-146, 154-210, 215-271, 276-342, 351-406, 410-466, 471-522, 527-593, 602-657, 662-714, 719-779, 788-843, 851-907, 912-968.

N-glycosylation site.

amino acids 121-124, 127-130, 294-297, 372-375, 492-495, 623-626, 682-685, 800-803, 823-826, 861-864, 911-914.

Protein kinase C phosphorylation site.

amino acids 54-56, 200-202, 253-255, 322-324, 329-331, 384-386, 434-436, 474-476, 573-575, 614-616, 627-629, 635-637, 1011-1013.

FIGURE 12B**Casein kinase II phosphorylation site.**

amino acids 90-93, 209-212, 370-373, 494-497, 541-544, 542-545, 577-560, 614-617, 668-671, 676-679, 684-687, 807-810, 914-917, 1011-1014.

Tyrosine kinase phosphorylation site.

amino acids 1000-1006, 1000-1007.

N-myristoylation site.

amino acids 8-13, 20-25, 176-181, 235-240, 260-265, 262-267, 289-294, 298-303, 536-541, 549-554, 563-568, 741-746, 839-844, 860-865, 864-869, 920-925, 934-939, 949-954, 979-984.

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 13-23, 173-183, 870-880.

Zinc carboxypeptidases, zinc-binding region 2 signature.

amino acids 538-548.

Cereal trypsin/alpha-amylase inhibitors family signature.

amino acids 132-154.

FIGURE 13A

DNA226179

CAAACGTTCCCAAATCTTCCAGTCGGCTTGCAGAGACTCCTTGCTCCCAGGAGATAACC
AGAAGCTGCATCTTATTGACAGATGGTCATCACATTGGTGAGCTGGAGTCATCAGATTGT
GGGCCCCGGAGTGAGGCTGAAGGGAGTGGATCAGAGCACTGCCTGAGAGTCACCTCTACT
TTCCTGCTACCGCTGCCTGTGAGCTGAAGGGGCTGAACCATACACTCCTTTTTCTACAAAC
CAGCTTGCAATTTTTCTGCCACAATGAGCGGGGAATCAATGAATTTAGCGATGTTTTTC
GACTCCAGTGAAGATTATTTTGTGTGAGTCAATACTTCATATTACTCAGTTGATTCTGAG
ATGTTACTGTGCTCCTTGCAGGAGGTCAGGCAGTTCTCCAGGCTATTTGTACCGATTGCC
TACTCCTTGATCTGTGTCTTTGGCCCTCTGGGGAAATTTCTGGTGGTGTATCACCTTTGCT
TTTTATAAGAAGGCCAGGCTCTATGACAGACGCTCTATCTCTTGAACATGGCCATTGCAGAC
ATCCTCTTTGTTCTTACTCTCCCATCTGCGGAGTGCAGTGCACCTGGTGCCTGGGTT
TTCAGCAATGCCACGTGCAAGTTGCTAAAAGGCATCTATGCCATCAACTTTAACTGCCGG
ATGCTGCTCCTGACTTGCATTAGCATGGACCGGTACATCGCCATTGTACAGGCGACTAAG
TCATTCCGGCTCCGATCCAGAACACTACCGCGCACGAAAATCATCTGCCCTTGTGTGTGG
GGGCTGTCACTCATCTCCAGCTCAACTTTTGTCTTCAACCAAAAATACAACACCCAA
GGCAGCGATGTCTGTGAACCCAAGTACCAGACTGTCTCGGAGCCCATCAGGTGGAAGCTG
CTGATGTTGGGGCTTGAGCTACTCTTTGGTTCTTTATCCCTTTGATGTTTATGATATTT
TGTTACACGTTTATTGTCAAACCTTGGTGCAAGCTCAGAAATCTAAAAGGCACAAAGCC
ATCCGTGTAATCATAGCTGTGGTGTCTGTGTTTCTGGCTTGTGAGATTCCTCATAACATG
GTCTGCTTGTGACGGCTGCAAATTTGGGTAAAATGAACCGATCCTGCCAGAGCGAAAAG
CTAATTGGCTATACGAAAAGTGTACAGAAGTCTGGCTTTCTGCACTGCTGCTGAAAC
CCTGTGCTCTACGCTTTTATTGGGCAGAAGTTCAGAAACTACTTTCTGAAGATCTTGAAG
GACCTGTGGTGTGTGAGAAGGAAGTACAAGTCTCAGGCTTCTCCTGTGCCGGGAGGTAC
TCAGAAAACATTTCTCGGCAGACCAGTGAGACCGCAGATAACGACAATGCCGTGCTCCTC
ACTATGAGTATAGAAAGCTGAGTCTCCCTAAGGCATGTGTGAAACATACTCATAGATGTTA
TGCAAAAAAAGTCTATGGCCAGGTATGCATGGAAAATGTGGGAATTAAGCAAAATCAAG
CAAGCCTCTCCTCGGGACTTAACTGCTCATGGGCTGTGTGATCTCTTCAGGGTGGG
GTGGTCTCTGATAGGTAGCATTTTTCCAGCACTTTGCAAGGAATGTTTTGTAGCTCTAGGG
TATATATCCGCCTGGCATTTCACAAAACAGCCTTTGGGAAATGCTGAATTAAGTGAAT
GTTGACAAATGTAAACATTTTCAGAAATATTCATGAAGCGGTACAGATCACAGTGTCTT
TTGGTTACAGCACAAAATGATGGCAGTGGTTTGA AAAACTAAAACAGAAAAAAAATGGAA
AGCCAACACATCACTCATTAGGCAAATGTTTAAACATTTTATCTATCAGAATGTTTA
TTGTTGCTGGTTATAAGCAGCAGGATTGGCCGGCTAGTGTTCCTCTCATTTCCTTTGA
TACAGTCAACAAGCCTGACCCTGTAAAATGGAGGTGGAAAGACAAGCTCAAGTGTTCACA
ACCTGGAAGTGTCTCGGGAAGAAGGGGACAATGGCAGAACAGGTGTGGTGACAATTGTC
ACCAATTGGATAAAGCAGCTCAGGTTGTAGTGGCCATTAGGAAACTGTGCGTTTTGCTTT
GATTTCCCTGGGAGCTGTTCTCTGTGCTGAGTGTCTCTTGTCTAAACGTCCATTAAAGCTG
AGAGTGTATGAAGACAGGATCTAGAATAATCTTGCTCACAGCTGTGCTCTGAGTGCCTA
GCGGAGTTCCAGCAAAACAAAATGGACTCAAGAGAGATTTGATTAATGAATCGTAATGAAG
TTGGGGTTTATTGTACAGTTTAAAATGTTAGATGTTTTTAAATTTTTTAAATAAATGGAA
ACTTTTTTTTTTTTTTAAAGAAAGCAACTTTACTGAGACAATGTAGAAAGAAGTTTTGTTC
CGTTTTCTTAAATGTGTTGAAGAGCAATGTGTGGCTGAAGACTTTTGTATGAGGAGCTG
CAGATTAGCTAGGGGACAGCTGGAATTTATGCTGGCTTCTGATAATTATTTAAAGGGGTC
TGAAAATTTGTGATGGAATCAGATTTTAAACAGCTCTCTTCAATGACATAGAAAATTCATGG
AACTCATGTTTTTAAAGGGCTATGTAATAATGAACATTAGAAAAATAGCAACTTGTGT

FIGURE 13B

TACAAAAATACAAACACATGTTAGGAAGGTACTGTCATGGGCTAGGCATGGTGGCTCACA
CCTGTAATCCCAGCATTGTTGGGAAGCTAAGATGGGTGGATCACTTGAGGTCAGGAGTTTG
AGACCAGCCTGGCCAACATGGCGAAACCCCTCTCTACTAAAAATACAAAAATTTGCCAGG
CGTGGTGGCGGGTGCCGTAAATCCCAGCTACTTGGGAGGCTGAGGCAAGAGAATCGCTTG
AACCAGGAGGCAGAGGTTGCAGTGAGCCGAGATCGTGCCATTGCACTCCAGCCTGGGTG
ACAGAGCGAGACTCCATCTCAAAAAAAAAAAAAAAAAA

FIGURE 14

DNA226179

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss,DNA226179

><subunit 1 of 1, 374 aa, 1 stop

><MW: 42508, pI: 9.34, NX(S/T): 6

MSGESMNFSDVFDSSSEDYFVSVNTSYYSVDSEMLLCSLQEVQRQFSRLFVPIAYS LICVFG
LLGNILVVITFAFYKKARSMTDVYLLNMAIADILFVLTLPFWAVSHATGAWVFSNATCKL
LKGIYAINFNCGMLLLTCISMDRYIAIVQATKSFRLRSRTLPRTKIICLVVWGLSVIIS
STFVFNQKYNTQGS DVCEPKYQTVSEPIRWKLLMLGLELLFGFFIPLMFMIFCYTFIVKT
LVQAQNSKRHKAIRVIIAVVLVFLACQIPHNMVLLVTAANLGKMNRSQCSEKLIGYTKTV
TEVLAFLHCCLNPVLYAFIQKFRNYFLKILKDLWCVRRKYKSSGFSCAGRYSENISRQT
SETADNDNASSF^TM

Signal sequence.

amino acids 1-43.

Transmembrane domain.

amino acids 48-68, 84-104, 123-143, 164-184, 204-224, 220-240, 245-265, 261-281, 298-318.

N-glycosylation site.

amino acids 7-10, 23-26, 115-118, 285-288, 355-358, 368-371.

Protein kinase C phosphorylation site.

amino acids 117-119, 153-155, 247-249, 290-292.

Casein kinase II phosphorylation site.

amino acids 14-17, 37-40, 79-82, 203-206, 299-302.

N-myristoylation site.

amino acids 60-65, 193-198.

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 256-266.

7 transmembrane receptor (rhodopsin family).

amino acids 63-316.

FIGURE 15

DNA226239

AGTCACAGAGGGAACACAGAGCCTAGTTGTA AACGGACAGAGACGAGAGGGGCAAGGGAG
GACAGTGGATGACAGGGAAGACGAGTGGGGGCAGAGCTGCTCAGGACC ATGGCTGAGGCC
ATCACCTATGCAGATCTGAGGTTTGTGAAGGCTCCCCGAAGAAGAGCATCTCCAGCCGG
TTAGGACAGGACCCAGGGGCTGATGATGATGGGGAATCACCTACGAGAATGTTCAAGTG
CCCGCAGTCTAGGGGTGCCCTCAAGCTTGGCTTCTTCTGTACTAGGGGACAAAGCAGCG
GTCAAGTCGGAGCAGCCAACTGCGTCCCTGGAGAGCCGTGACGTCAACCAGCTGTCCGGCCGG
ATTCTCCCCTGCCGCACAACCTGCGTACCTCTGCTCGGCTGCTCCTCACCTGC
CTGCTGTTAGGAGTGACCGCCATCTGCCCTGGGAGTGCCTATCTGCAGGTGCTCTCAGCAG
CTCCAGCAGACGAACAGGGTTCTGGAAGTCACTAACAGCAGCCTGAGGCAGCAGCTCCGC
CTCAAGATAACGCAGCTGGGACAGAGTGCAGAGGATCTGCAGGGTCCAGGAGAGAGCTG
GCGCAGAGTCAGGAAGCACTACAGGTGGAACAGAGGGCTCATCAGCGGCCGAAGGGCAG
CTACAGGCCTGCCAGGCAGACAGACAGAAGACGAAGGAGACCTTGCAAAGTGAGGAGCAA
CAGAGGAGGGCCTTGGAGCAGAAGCTGAGCAACATGGAGAACAGACTGAAGCCCTTCTTC
ACATGCCGCTCAGCAGACACCTGCTGTCCGTCCGGATGGATAATGCATCAGAAAAGCTGC
TTTTACATCTCACCTTACTTCAAAAAATTGGCAGGAGAGCCAAAAACAATGTGAAACTCTG
TCTTCCAAGCTGGCCACATTCAGTGAAATTTATCCACAATCACACTCTTACTACTTCTTA
AATTCAGTGTGGCCAAATGGTGGTTCAGGGAATTCATATTGGACTGGCCCTCAGCTCTAAC
AAGGATTGGAAGTTGACTGATGATACACAACGCCTAGGACTTATGCTCAAAGCTCAAAA
TGTAACAAGGTACATAAACTTGGTCAATGGTGGACTGGAGTCAGAGTCATGTAGAAGT
TCTCTCCCTACATCTGTGAGATGACAGCTTTCAGGTTTCAGAT TAGGACAGTCCTTG
CACTGAGTTGACACTCATGCCAACAGAACCCTGTGCCCTCCTTCTAACCTGAGGCCTG
GGTTCCTCAGACCATCTCCTTCATTCGGGCAGTGCCAGCCACCGCTGACCCACACCT
GACACTCCAGCCAGTCTGCTGCCTGCTCCCTCTTCTGAAACTGGACTGTTCTGGGAA
AAGGGTGAAGCCACCTCTAGAAGGGACTTTGGCCTCCCCCAAGA ACTTCCATGGTAGA
ATGGGGTGGGGAGGAGGGCGCAGGGCTGAGCGGATAGGGGCGGCCCGGAGCCAGCCAG
GCAGTTTTATTGAAATCTTTTTAAATAATTG

FIGURE 16

DNA226239

><subunit 1 of 1, 359 aa, 1 stop

><MW: 40220, pI: 8.70, NX(S/T): 1

MAEAITYADLRFVKAPLKKSISSRLGQDPGADDDGEITYENVQVPAVLGVPSSLASSVLG
DKAAVKSEQPTASWRAVTSFAVGRILPCRTTCLRYLLGLLLTCLLLGVTAICLGVRYLQ
VSQQLQQTNRVLEVTNSSLRQQLRLKITYLQSAEDLQGSRRRELAQSQEALQVEQRAHQ
AEGQLQACQADRQKTKETLQSEEQRRRALEQKLSNMENRLKPFFTCGSADTCCPSGWIMH
QKSCFYISLTSKNWQESQKQCETLSSKLATFSEIYPQSHSYFFLNLLPNGGSGNSYWTG
LSSNKDWKLTDDTQTRTRYAQSSKCNKVHKTWSWWTLESESCRSSLPYICEMTAFRFPD

Signal sequence.

amino acids 1-22.

Transmembrane domain.

amino acids 91-111.

N-glycosylation site.

amino acids 136-139.

Protein kinase C phosphorylation site.

amino acids 22-24, 73-75, 128-130, 138-140, 160-162, 250-252, 257-259, 265-267, 303-305, 313-315, 322-324, 341-343.

Casein kinase II phosphorylation site.

amino acids 6-9, 153-156, 160-163, 214-217, 270-273, 303-306.

N-myristoylation site.

amino acids 26-31, 49-54, 99-104, 183-188, 227-232, 291-296, 292-297, 300-305.

Leucine zipper pattern.

amino acids 86-107, 93-114, 143-164, 150-171.

Lectin C-type domain.

amino acids 250-352.

FIGURE 17

DNA226394

GGCACGAGGGTCCGCAAGCCCGGCTGAGAGCGCGCCATGGGGCAGGCGGGCTGCAAGGGG
CTCTGCCTGTCTGTTCGACTACAAGACCGAGAAGTATGTCATCGCCAAGAAACAAGAAG
GTGGGCCTGTCTACCGGCTGCTGCAGGCCCTCCATCCTGGCGTACCTGGTCTATGGGTG
TTCTTGATAAAGAAGGGTTACCAAGACGTCGACACGTCCTGCAGAGTGTGTATCACC
AAAGTCAAGGGCGTGGCCTTACCAACACCTCGGATCTTGGGCAGCGGATCTGGGATGTC
GCCGACTACGTCAATCCAGCCCAGGGAGAGAACGTCCTTTTGTGGTCACCAACCTGATT
GTGACCCCCAACCAGCGGCAGAACGTCGTGTCTGAGAATGAAGGCATTCTGATGGCGCG
TGCTCCAAGGACAGCGACTGCCACGCTGGGGAAGCGGTTACAGCTGGAAACGGAGTGAAG
ACCGGCCGCTGCCTGCGGAGAGGGAACCTGGCCAGGGGCACCTGTGAGATCTTTCCTGG
TGCCCGTTGGAGACAAGCTCCAGGCGGAGGAGCCATTCTGAAGGAGGCCGAAGACTTC
ACCATTTTCATAAAGAACCAATCCGTTTCCCCAAATCACTTCTCCAAAAAATGTG
ATGGACGTCAGGACAGATCTTTCTGAAATCATGCCACTTTGGCCCCAAGAACCACTAC
TGCCCCATCTCCGACTGGGCTCCATCGTCCGCTGGGCCGGGAGCGACTTCCAGGATATA
GCCCTGCGAGGTGGCGTGATAGGAATTAATATTGAATGGAACGTGATCTTGATAAAGCT
GCCTCTGAGTGCCACCCTCACTATCTTTTAGCCGCTGGACAATAAACTTCAAAGTCT
GTCTCTCCGGGTACAACCTCAGATTTGCCAGATATTACCGAGACGCAGCCGGGGTGGAG
TTCCGCACCCTGATGAAAGCCTACGGGATCCGCTTTGACGTGATGGTGAACGGCAAGGGT
GCTTTCTTCTGCGACCTGGTACTCATCTACCTCATCAAAAAGAGAGATTTTACCCTGAC
AAGAAGTACGAGGAAGTGAGGGGCTAGAAGACAGTTCCAGGAGGCCGAGGACGAGGCA
TCGGGGCTGGGGCTATCTGAGCAGCTCACATCTGGGCCAGGGCTGTGGGGATGCCGGAG
CAGCAGGAGCTGCAGGAGCCACCCGAGGCGAAGCGTGGAAGCAGCAGTCAGAAGGGGAAC
GGATCTGTGTGCCACAGCTCCTGGAGCCCCACAGGAGCAGTGAATTGCCTCTGCTTAC
GTTTCAGGCCCTGTCTAAACCCAGCCGTCTAGCACCCAGTGATCCCATGCCTTTGGGAAT
CCCAGGATGCTGCCAACGGGAAATTTGTACATTGGGTGCTATCAATGCCACATCACAGG
GACCAGCCATCACAGAGCAAAGTGACCTCCACGTCGTGATGCTGGGGTCATCAGGACGGAC
CCATCATGGCTGTCTTTTGGCCCCACCCCTGCCGTGATCTCTCTTTCTCCGTGGCTG
GCTTCCCGCACTAGGGAACGGGTGTAAATGGGGAACATGACTTCCCTCCGGAGTCCCTG
AGCACCTCAGCTAAGGACCGCAGTCCCTGTAGAGTTCCTAGATTACCTCACTGGGAATA
GCATTGTGCGTGTCCGAAAAGGGCTCCATTTGGTTCAGCCCACTCCCTCTGCAAGTG
CCACAGCTTCCCTCAGAGCATACTCTCCAGTGGATCCAAGTACTCTCTCTCTAAAGACA
CCACCTTCTGCCAGCTGTTTGGCCCTTAGGCCAGTACACAGAATTAAGTGGGGGAGATG
GCAGACGCTTCTGGGACCTGCCCAAGATATGTATTCTCTGACACTCTTATTTGGTCATA
AAAAAATAAATGGTGTCAATTTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 18

DNA226394

><subunit 1 of 1, 422 aa, 1 stop
><MW: 47187, pI: 8.40, NX(S/T): 3

MGQAGCGKGLCLSLFDYKTEKYVIAKNKKVGLLYRLLQASILAYLVVWVFLIKKGYQDVDT
SLQSAVITKVKGVAFNTSDLGQRIWDVADYVIPAQGENVFFVVTNLIVTPNQQRNVCAE
NEGIPDGACSKSDSDCHAGEAVTAGNGVKTGRCLRRGNLARGTCEIFAWCPLETSSRPEEP
FLKEAEDPTIFIKNHIRFPKFNFSKNNVMDVKDRSFLKSCHFGPKNHYCPIFRLGSIVRW
AGSDFQDIALRGGVIGINIEWNCDLKAASECHPHYSFSRLDNKLSKSVSSGYNFRFARY
YRDAAGVEFRTLKAYGIRFDVMVNGKGAFFCDLVLIIYLIKKREFYRDKKYEVRGLED
SQEAEDEASGLGLSEQLTSGPGLLMPEQOELQEPPEAKRGSSSQKNGSVCPQLLEPHR
ST

N-glycosylation site.

amino acids 77-80, 202-205, 408-411.

Glycosaminoglycan attachment site.

amino acids 369-372, 379-382.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 399-402.

Protein kinase C phosphorylation site.

amino acids 18-20, 149-151, 174-176, 404-406.

Casein kinase II phosphorylation site.

amino acids 12-15, 175-178, 279-282, 360-363.

Tyrosine kinase phosphorylation site.

amino acids 84-91.

N-myristoylation site.

amino acids 2-7, 8-13, 72-77, 123-128, 146-151, 252-257, 328-333, 356-361,
370-375.

ATP P2X receptor.

amino acids 14-364.

FIGURE 19

DNA226423

AACTCATTCTGAAGAGGCTGACGATTTTACTGTCTCATTFTTTTCCTTTCTCCAGA ATGG
GTTCTGGGTGGGTCCCCTGGGTGGTGGCTCTGCTAGTGAATCTGACCCGACTGGATTCCCT
CCATGACTCAAGGCACAGACTCTCCAGAAGATTTTGTGATTCAGGCAAAGGCTGACTGTT
ACTTCACCAACGGGACAGAAAAGGTGCAGTTTGTGGTCAGATTCATCTTTAACTTGGAGG
AGTATGTACGTTTCGACAGTGATGTGGGGATGTTTGTGGCATTGACCAAGCTGGGGCAGC
CAGATGCTGAGCAGTGGAAACAGCCGGCTGGATCTCTTGGAGAGGAGCAGACAGGCCGCTGG
ATGGGGTCTGTAGACACAACCTACAGGCTGGGCGCACCCCTTCACTGTGGGGAGAAAAGTGC
AACCAGAGGTGACAGTGTACCCAGAGAGGACCCCACTCCTGCACCAGCATAATCTGCTGC
ACTGCTCTGTGACAGGCTTCTATCCAGGGATATCAAGATCAAGTGGTTCTGAATGGGC
AGGAGGAGAGAGCTGGGGTCACTGTCCACTGGCCCTATCAGGAATGGAGACTGGACCTTTC
AGACTGTGGTGATGCTAGAAATGACTCCTGAACTGGACATGTCTACACCTGCCTTGTCC
ATCACTCCAGCCTGCTGAGCCCTGTTTCTGTGGAGTGGAGAGCTCAGTCTGAATATTCTT
GGAGAAAGATGCTGAGTGGCATTGCAGCCTTCCTACTTGGGCTAATCTTCTTCTGGTGG
GAATCGTCATCCAGCTAAGGGCTCAGAAAGGATATGTGAGGACGCAGATGTCTGGTAATG
AGGTCTCAAGAGCTGTTCTGCTCCCTCAGTCATGC TAAGGTCCTCACTAAGCTTGTCTC
TCTGGAGCCTGAAGTAGTGATGAGTAGTCTGGGCCCTGGGTGAGGTAAAGGACATTCATG
AGGTCAATGTTCTGGGAATAACTCTCTTCCCTGATCCTTGGAGGAGCCCGAACTGATTCT
GGAGCTCTGTGTTCTGAGATCATGCATCTCCACCCATCTGCCCTTCTCCCTTCTACGTG
TACATCATTAAATCCCCATTGCCAAGGGCATTGTCCAGAAACTCCCCTGAGACCTTACTCC
TTCCAGCCCCAAATCATTTACTTTTCTGTGGTCCAGCCCTACTCCTATAAGTCATGATCT
CCAAAGCTTTCTGTCTTCCAAGTGCAGTCTCCACAGTCTTCCAGAAGACAAATGCTCAGGT
AGTCACTGTTTCTTTTCACTGTTTTTAAAAACCTTTTATTGTCAAATAAAATGGAGATA
CA

FIGURE 20

DNA226423

><subunit 1 of 1, 273 aa, 1 stop
><MW: 30822, pI: 6.72, NX(S/T): 2
MGSWVWPVVALLVNLTRLSSMTQGTDSPEDFVIQAKADCYFTNGTEKVQFVVRFI FNL
EEYVRFSDVGMFVALTKLGQPDAEQWNSRLDLLERSRQAVDGVCRHNYRLGAPFTVGRK
VQPEVTVPERTPLLHQHLLHCSVTGFYPGDIKIKWFLNGQEERAGVMSTGPIRNGDWT
FQTVVMLEMTPELGHVYTCLVDHSSLLSPVSVEWRAQSEYSWRKMLSGIAAFLLGLIFLL
VGI VIQLRAQKGYVRTQMSGNEVSRVLLPQSC

Signal sequence.

amino acids 1-21.

Transmembrane domain.

amino acids 225-245.

N-glycosylation site.

amino acids 15-18, 45-48.

Protein kinase C phosphorylation site.

amino acids 47-49, 221-223.

Casein kinase II phosphorylation site.

amino acids 17-20, 29-32, 89-92, 259-262.

Tyrosine kinase phosphorylation site.

amino acids 120-128.

N-myristoylation site.

amino acids 71-76, 80-85, 112-117, 167-172, 260-265.

Amidation site.

amino acids 117-120.

Leucine zipper pattern.

amino acids 226-247.

Immunoglobulins and major histocompatibility complex proteins signature.

amino acids 197-203.

Class II histocompatibility antigen, beta.

amino acids 39-116.

Immunoglobulin domain.

amino acids 136-201.

FIGURE 21A

DNA227781

GCTGCCACCTCTCTAGAGGCACCTGGCGGGAGCCTCTCAACATAAGACAGTGACCAGTC
TGGTGACTCACAGCCGGCACAGCCATGAACTACCCGCTAACGCTGGAAATGGACCTCGAG
AACCTGGAGGACCTGTTCTGGGAACCTGGACAGATTGGACAACATAAACGACACCTCCCTG
GTGGAAAATCATCTCTGCCCTGCCACAGAGGGTCCCCTCATGGCCTCCTTCAAGGCCGTG
TTCGTGCCCGTGGCCTACAGCCTCATCTTCTCCTGGGCGTGATCGGCAACGTCCTGGTG
CTGGTGATCCTGGAGCGGCACCGGCAGACACGCAGTTCACGGAGACCTTCTGTTCCAC
CTGGCCGTGGCCGACCTCCTGCTGGTCTTCATCTTGCCCTTTGGCGTGGCCGAGGGCTCT
GTGGGGTGGGTCTGGGGACCTTCTCTGCAAACTGTGATTGCCCTGCACAAAGTCAAC
TTCTACTGCAGCAGCCTGCTCCTGGCCTGCATCGCCGTGGACCGCTACCTGGCCATTGTC
CACGCCGTCCATGCCTACCGCCACCGCCGCCTCCTTCCATCCACATCACCTGTGGGACC
ATCTGGCTGGTGGGGTCTCCTTGGCCTTGCCAGAGATTCTCTTCGCCAAAGTCAGCCAA
GGCCATCAACAACACTCCTGCCACGTTGCACCTTCTCCCAAGAGAACCAAGCAGAAAACG
CATGCCCTGGTTACCTCCCGATTCTCTACCATGTGGCGGGATTCTTGCTGCCCATGCTG
GTGATGGGCTGGTGCTACGTGGGGGTAGTGCACAGGTTGCGCCAGGCCAGCGGCGCCCT
CAGCGGCAGAAGGCAGTCAGGGTGGCCATCCTGGTGACAAGCATCTTCTTCTCTGCTGG
TCACCCCTACCACATCGTCATCTTCTGGACACCCTGGCGAGGCTGAAGCCGTGGACAAT
ACCTGCAAGCTGAATGGCTCTCTCCCGTGGCCATCACCATGTGTGAGTTCCTGGGCCGTG
GCCACTGCTGCCTCAACCCCATGCTCTACACTTTCGCCGGCGTGAAGTTCGCGAGTGAC
CTGTCCGGCTCCTGACCAAGCTGGGCTGTACCGCCCTGCCTCCCTGTGCCAGCTCTTC
CCTAGCTGGCGCAGGAGCAGTCTCTCTGAGTCAGAGAATGCCACCTCTCTCACCCAGTTC
TAGGTCCCAGTGTCCCCTTTTATTGCTGCTTTTCTTGGGGCAGGCAGTGATGCTGGATG
CTCCTTCCAACAGGAGCTGGGATCCTAAGGGCTCACCGTGGCTAAGAGTGTCTTAGGAGT
ATCCTCATTTGGGGTAGCTAGAGGAACCAACCCATTTCTAGAACATCCCTGCCAGCTCT
TCTGCCGGCCCTGGGGCTAGGCTGGAGCCAGGGAGCGGAAAGCAGCTCGAAGGCACAGT
GAAGGCTGTCTTACCATCTGCACCCCTGGGCTGAGAGAACCTCACGCACCTCCCAT
CCTAATCATCCAATGCTCAAGAAAACACTTCTACTTCTGCCCTTGCCAAACGGAGAGCGCC
TGCCCTCCAGAACACACTCCATCAGCTTAGGGGCTGCTGACCTCCACAGCTTCCCCCTC
TCTCTCTGCCACCTGTCAAAACAAAGCCAGAAGCTGAGCACCAGGGGATGAGTGGAGG
TTAAGGCTGAGGAAAGGCCAGCTGGCAGCAGAGTGTGGCTTCGGACAACCTCAGTCCCTAA
AAACACAGACATTTGCCAGGCCCCCAAGCCTGCAGTCATCTTGACCAAGCAGGAAGCTC
AGACTGGTTGAGTTCAGGTAGCTGCCCCTGGCTCTGACCGAAACAGCGCTGGGTCCACCC
CATGTACCGGATCCTGGGTGGTCTGCAGGCAGGGCTGACTCTAGGTGCCCTTGGAGGCC
AGCCAGTGACCTGAGGAAGCGTGAAGGCCGAGAAGCAAGAAAGAAACCCGACAGAGGGAA
GAAAAGAGCTTCTTCCCGAACCCCAAGGAGGGAGATGGATCAATCAAACCCGGCTGTCC
CCTCCGCCAGGCGAGATGGGGTGGGGGAGAACTCTAGGGTGGCTGGGTCCAGGGGAT
GGGAGGTTGTGGGCATTGATGGGGAAGGAGGCTGGCTGTCCCTCTCACTCCCTTCCC
ATAAGCTATAGACCCGAGGAACTCAGAGTCGGAACGGAGAAAGGTGGACTGGAAGGGGC
CCGTGGGAGTCATCTCAACCATCCCCTCCGTTGGCATCACCTTAGGCAGGGAAGTGTAAAG
AAACACACTGAGGCAGGAACCTCCAGGCCAGGAAGCCGTGCCCTGCCCCGTGAGGATG
TCACTCAGATGGAACCGCAGGAAGCTGCTCCGTGCTTGTTCCTCACTGGGGTGTGGGA
GGCCCGTCCGGCAGTTCGGGTGCTCCCTACCACCTCCCAGCCTTTGATCAGGTGGGGA
GTCAGGGACCCCTGCCCTTGTCCCCTCAAGCCAAGCAGCCAAGCTCCTTGGGAGGCCCC
ACTGGGAAATAACAGCTGTGGCTCACGTGAGAGTGTCTTACGGCAGGACAACGAGAAA
GCCCTAAGACGTCCCTTTTTCTCTGAGTATCTCCTCGCAAGCTGGGTAATCGATGGGGA
GTCTGAAGCAGATGCAAGAGGCAGAGGATGGATTTTGAATTTCTTTTTAATAAAAAGG

FIGURE 21B

CACCTATAAAACAGGTCAATACAGTACAGGCAGCACAGAGACCCCCGGAACAAGCCTAAA
AATTGTTTCAAATAAAAACCAAGAAGATGTCTTCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 22

DNA227781

><subunit 1 of 1, 372 aa, 1 stop

><MW: 41955, pI: 8.58, NX(S/T): 4

MNYPLTLEMDLENLEDFWELDRLDNYNDTSLVENHLCPATEGPLMASFKAVFVPVAYSL
IFLLGVIGNVLVLVILERHRQTRSSTETFLFHLAVADLLLVLFPFAVAEGSVGWVLGTF
LCKTVIALHKVNFYCSSLLLACIAVDRYLAIVHAVHAYRHRRLLSIHITCGTIWLVGFL
ALPEILPAKVSQGHNNLSLPRCTFSQENQAETHAWFTSRFLYHVAGFLLPMLVMGWCYVG
VVHRLRQAQRPRQKAVRVAILVTSIFFLCWSPYHIVIFLDTLARKAVDNTCKLNGSL
PVAITMCEFLGLAHCCCLNPMPLYTFAGVKFRSRLSRLTLKLGCTGPASLCQLFPSWRRSSL
SESENATSLTTF

Transmembrane domain.

amino acids 52-72, 90-110, 129-149, 166-186, 219-239, 259-279, 299-319.

N-glycosylation site.

amino acids 28-31, 196-199, 297-300, 365-368.

cAMP- and cGMP-dependent protein kinase.

amino acids 356-359.

Protein kinase C phosphorylation site.

amino acids 48-50, 217-219, 293-295, 354-356.

Casein kinase II phosphorylation site.

amino acids 31-34, 84-87, 305-308, 359-362, 361-364.

N-myristoylation site.

amino acids 65-70, 118-123, 311-316.

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 132-142.

FIGURE 23

DNA 227879

AGTGGCTCTACTTTTCAGAAGAAAGTGTCTCTCTTCTCCTGCTTAAACCTCTGTCTCTGACGG
TCCCTGCCAATCGCTCTGGTCGACCCCAACACTAGGAGGACAGACACAGGCTCCAAAC
TCCACTAACCAGAGCTGTGATTGTGCCCCTGAGTGGACTGCGTTGTTCAGGGAGTGAGTG
CTCCATCATCGGGAGAATCCAAGCAGGACCGCCATGGAGGAAGGTCAATATTCAGAGATC
GAGGAGCTTCCCAGGAGGCGGTGTTGCAGGCGTGGGACTCAGATCGTGCTGCTGGGGCTG
GTGACCGCCGCTCTGTGGGCTGGGCTGCTGACTCTGCTTCTCCTGTGGCACTGGGACACC
ACACAGAGTCTAAAACAGCTGGAAGAGAGGGCTGCCCGGAACGCTCTCAAGTTTCCAAG
AACTTGGAAAGCCACCACGGTGACCAGATGGCGCAGAAATCCCAGTCCACGCAGATTTCA
CAGGAACCTGGAGGAACCTCGAGCTGAACAGCAGAGATTGAAATCTCAGGACTTGGAGCTG
TCCTGGAACCTGAACGGGCTTCAAGCAGATCTGAGCAGCTTCAAGTCCCAGGAATTGAAC
GAGAGGAACGAAGCTTCAGATTTGCTGGAAGACTCCGGGAGGAGGTGACAAAGCTAAGG
ATGGAGTTGCAGGTGTCCAGCGGCTTTGTGTGCAACACGTGCCCTGAAAAGTGGATCAAC
TTCCAACGGAAGTGTACTACTTTCGGCAAGGGCACCAAGCAGTGGGTCCACGCCCGGTAT
GCCTGTGACGACATGGAAGGGCAGCTGGTCAGCATCCACAGCCCAGGAGCAGGACTTC
CTGACCAAGCATGCCAGCCACACCGGCTCCTGGATTGGCCTTCGGAACCTGGACCTGAAG
GGAGAGTTTATCTGGGTGGATGGGAGCCATGTGGACTACAGCAACTGGGCTCCAGGGGAG
CCCACCAGCCGAGCCAGGGCGAGGACTGCGTGATGATGCGGGGCTCCGGTCTGCTGGACC
GACGCCCTCTGCGACCGTAAGCTGGGCGCCTGGGTGTGCGACCGGCTGGCCACATGCACG
CCGCCAGCCAGCGAAGGTTCCGCGGAGTCCATGGGACCTGATTCAAGACCAGACCCCTGAC
GGCCGCCCTGCCACCCCTCTGCCCCCTCTCCACTCTTGAGCATGGATACAGCCAGGCCCA
GAGCAAGACCCCTGAAGACCCCAACCAACCGCCTAAAAGCCTCTTTGTGGCTGAAAGGTCC
CTGTGACATTTTCTGCCACCCAAACGGAGGCAGCTGACACATCTCCCGCTCCTCTATGGC
CCCTGCCTTCCCAGGAGTACACCCCAACAGCACCCCTCTCCAGATGGGAGTGCCCCAACA
GCACCCCTCTCCAGATGAGAGTTACACCCCAACAGCACCCCTCTCCAGATGCAGCCCCATCT
CCTCAGCACCCAGGACCTGAGTATCCCCAGCTCAGGGTGGTGTGATCCTCCTGTCCAGCC
TGCATCAATAAAATGGGGCAGTGATGGCC

FIGURE 24

DNA 227879

><subunit 1 of 1, 321 aa, 1 stop

><MW: 36456, pI: 5.52, NX(S/T): 1

MEEGQYSEIEELPRRRCCRRGTQIVLLGLVTAALWAGLLTLLLLLWHWDTTQSLKQLEERA
ARNVSVQSKNLESHHGDOMAQKSQSTQISQEEELRAEQRLKSQDLELSWNLNGLQADL
SSFKSQELNERNEASDLLERLREEVTKLRMELQVSSGFVNTCPEKWINFQRKCYFYGKG
TKQVWHARYACDDMEGQLVSIHSPPEEQDPLTKHASHTGSWIGLRNLDLKGEFIWVDGSHV
DYSNWAPGEPTSRSQGEDCVMMRGSGRWTDAFCDRKLGAWVCDRLATCTPPASEGSAESM
GPDSRPDPDGRLLPTPSAPLHS

Signal sequence.

amino acids 1-36.

Transmembrane domain.

amino acids 23-43.

N-glycosylation site.

amino acids 63-66.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 19-22.

Protein kinase C phosphorylation site.

amino acids 52-54, 122-124, 251-253, 265-267.

Casein kinase II phosphorylation site.

amino acids 7-10, 162-165, 203-206, 238-241, 254-257, 304-307.

FIGURE 25

getseq sst.DNA256363

AGAGATGGGGACGGAGGCCACAGAGCAGGTTTCTGGGGCCATTACTCTGGGGATGAAGA
GGACGCATACTCGGCTGAGCCACTGCCGGAGCTTTGCTACAAGGCCGATGTCCAGGCCTT
CAGCCGGGCCTTCCAACCCAGTGTCTCCCTGACCGTGGCTGCGCTGGGTCTGGCCGGCAA
TGGCCTGGTCTGGCCACCCACCTGGCAGCCCGACGCGCAGCGCGCTCGCCACCTCTGC
CCACCTGCTCCAGCTGGCCCTGGCCGACCTCTTGCTGGCCCTGACTCTGCCCTTCGCGGC
AGCAGGGGCTCTTCAGGGCTGGAGTCTGGGAAGTGCCACCTGCCGCACCATCTCTGGCCT
CTACTCGGCCTCCTTCCACGCCGGCTTCTCTTCTGGCCTGTATCAGCGCCGACCGCTA
CGTGGCCATCGCGCGAGCGCTCCAGCCGGGCCGCGGCCCTCCACTCCCGGCCGCGCACA
CTTGGTCTCCGTCACTCGTGTGGCTGCTGTCACTGCTCCTGGCGCTGCCTGCGCTGCTCTT
CAGCCAGGATGGGCAGCGGAAGGCCAACGACGCTGTGCTCATCTTCCCCGAGGGCCT
CACGCAGACGGTGAAGGGGGCAGCGCCGTGGCGCAGGTGGCCCTGGGCTTCGCGCTGCC
GCTGGGCGTCATGGTAGCCTGTACGCGCTTCTGGGCCGACGCTGCTGGCCGCCAGGGG
GCCCCAGCGCCGGCGTGGCTGCGCGTGGTGGCTCTGGTGGCGGCCCTTCGTGGTGTCT
GCAGCTGCCCTACAGCCTCGCCCTGCTGCTGGATACTGCCGATCTACTGGCTGCGCGGA
GCGGAGCTGCCCTGCCAGCAAACGCAAGGATGTGCACTGCTGGTGACCAGCGGCTTGGC
CCTCGCCCGCTGTGGCCTCAATCCCGTTCTCTACGCTTCTTGGCCCTGCGCTTCCGCCA
GGACCTGCGGAGGCTGTACGGGGTGGGAGCTCGCCCTCAGGGCCTCAACCCCGCCGCGG
CTGCCCCCGCCGGCCCGCTTTCTTCTGCTCAGCTCCCACGGAGACCCACAGTCTCTC
CTGGGACAACTAGGGCTGCGAATCTAGAGGAGGGGGCAGGCTGAGGGTCTGGGAAAGGG
GAGTAGGTGGGGGAACACTGAGAAAGAGGCAGGGACCTAAAGGGACTACCTCTGTGCCTT
GCCACATTAATTGATAACATGGAAATGAAAAAAAAAAAAAAAAA

FIGURE 26

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA256363
><subunit 1 of 1, 362 aa, 1 stop
><MW: 38400, pI: 10.04, NX(S/T): 0
MGTEATEQVSWGHSYSGDEEDAYSAEPLPELCYKADVQAFSRAFPQPSVSLTVAALGLAGNG
LVLATHLAARRAARSPTS AHL LQLALADLLLALTL PFAAAGALQGWSLGSATCRTISGLY
SASFHAGFLFLACISADRYVAIARALPAGPRPSTPGRAHLVSVIVWLLSLLLALPALLFS
QDGQREGQRRCRLIFPEGLTQTVKGASAVAQVALGFALPLGVMVACYALLGRTLLAARGP
ERRRALRVVVALVAAFVVLQLPYSLALLLDTADLLAARERSCPASKRKDVALLVTSGLAL
ARCGLNPLYAFGLRFRQDLRRLRLGGSSPSGPPRRGCPRRRRLSSCSAPTETHSLSW
DN
```

Transmembrane domain.

Amino acids 43-63, 80-100, 119-139, 158-178, 209-229, 249-269, 291-311.

Seven-transmembrane receptor domain.

Amino acids 58-310.

Protein kinase C phosphorylation site.

Amino acids 112-114, 202-204, 285-287.

Casein kinase II phosphorylation site.

Amino acids 15-18.

N-myristoylation site.

Amino acids 2-7, 55-60, 60-65, 101-106, 109-114, 118-123, 183-188, 187-192, 198-203, 221-226, 297-302, 328-333.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 123-133, 216-226.

FIGURE 27

DNA332467

CCTCGGTTCTATCGATTGAATTCATGAAGACATTGCCTGCCATGCTTGGAACTGGGAAAT
TATTTTGGGTCTTCTTCTTAATCCCATATCTGGACATCTGGAACATCCATGGGAAAGAAT
CATGTGATGTACAGCTTATATAAAGAGACAATCTGAACACTCCATCTTAGCAGGAGATC
CCTTTGAACTAGAATGCCCTGTGAAATACTGTGCTAACAGGCCTCATGTGACTTGGTGCA
AGCTCAATGGAAACAACATGTGTAAAACCTGAAGATAGACAAACAAGTTGGAAGGAAGAGA
AGAACATTTCATTTTTCATTCTACATTTTGAACCAGTGCTTCCATGACAATGGGTCAT
ACCGCTGTTCTGCAAATTTTCAGTCTAATCTCATTGAAAGCCACTCAACAACCTTTTATG
TGACAGATGTAAAAAGTGCTTCAGAACGACCCCTCCAGGACGAAATGGCAAGCAGACCCCT
GGCTCCTGTATAGTTTACTTTCCTTTGGGGGGATTGCCTCTACTCATCACTACCTGTTTCT
GCCTGTTCTGCTGCCTGAGAAGGCACCAAGGAAAGCAAAATGAACTCTCTGACACAGCAG
GAAGGGAAATTAACCTGGTTGATGCTCACCTTAAGAGTGAGCAAACAGAAGCAAGCACCA
GGCAAAATTCCCAAGTACTGCTATCAGAAACTGGAATTTATGATAATGACCCTGACCTTT
GTTTCAGAAATGCAGGAAGGGTCTGAAGTTTATTCTAATCCATGCCTGGAAGAAAACAAC
CAGGCATTGTTTATGCTTCCCTGAACCATCTGTGTCATTGGACTGAACTCAAGACTGGCAA
GAAATGTAAAAGAAGCACCAACAGAATATGCATCCATATGTGTGAGGAGT TAAGGATCCT
CTAGAGTCGACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAA
GTGTTACAAATAACAATAATATTTCTCAATTTGAGAATTTTTACTTTAGAAATGTTC
TGTTAGTGCTTGGGTCTGAAGGGTCCATAGGACAAATGATTTAAAT

FIGURE 28

DNA332467

><subunit 1 of 1, 289 aa, 1 stop

><MW: 32781, pI: 6.27, NX(S/T): 4

MKTLPAMLGTGKLFWVFFLIPLYLDIWNHIGKESCDVQLYIKRQSEHSILAGDPFELECPV
KYCANRPHVTWCKLNGTTCVKLEDRQTSWKEEKNISFFILHFEPVLPNDNGSYRCSANFQ
SNLIESHSTTLVYVTDVKSASERPSKDEMASRPWLLYSLLPLGGLPLLITTCFCLFCCLRR
HQGKQNELSDTAGREINLVDAHLKSEQTEASTRONSQVLLSETGIYDNDPDLCFRMQEGS
EVYSNPCLEENKPGIVYASLNHSVIGLNSRLARNVKEAPTEYASICVRS

Transmembrane domain.

amino acids 153-173.

N-glycosylation site.

amino acids 75-78, 94-97, 110-113, 261-264.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 41-44.

Protein kinase C phosphorylation site.

amino acids 10-12, 88-90, 112-114, 140-142, 211-213.

Casein kinase II phosphorylation site.

amino acids 88-91, 138-141, 144-147.

Tyrosine kinase phosphorylation site.

amino acids 31-39.

N-myristoylation site.

amino acids 111-116, 224-229, 254-259.

Immunoglobulin domain.

amino acids 51-117.

FIGURE 29

DNA335922

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACC ATGA
AGCTCTTGTGGCAGGTAAGTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTTCG
TCTACCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCTCAGCCG
GGCCCCAGAACTGCCCTCCGTTTGTCTCGTGCAGTAACCAGTTCAGCAAGGTGGTGTGCA
CGCGCCGGGGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACC
TCATGGAGAACAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGG
AGGTCTGCAGTTGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGCCTTCAACGGCC
TGGCCAGCTCAACACCTGGAGCTGTTGACAACTGGCTGACAGTCATCCCTAGCGGGG
CCTTTGAATACCTGTCCAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCA
TCCCCTCTACGCCTTCAACCGGGTGCCTCCCTCATGCGCTGGACTTGGGGGAGCTCA
AGAAGCTGGAGTATATCTCTGAGGGAGCTTTTGGGGGCTGTTCAACCTCAAGTATCTGA
ACTTGGGCATGTGCAACATTAAGACATGCCAATCTCACCCCTGGTGGGGCTGGAGG
AGCTGGAGATGTCAGGGAACCACTTCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGA
GCTCCCTCAAGAAGCTCTGGGTCACTGAACTCACAGGTCAGCCTGATTGAGCGGAATGCTT
TTGACGGCTGGCTTCACTTGTGGAACCAACTTGGCCACAATAACCTCTCTTCTTTGC
CCCATGACCTCTTTACCCCGCTGAGGTACCTGGTGGAGTTGCATCTACACCACAACCTT
GGAAGTGTGATTGTGACATTTCTGTGGCTAGCCTGGTGGCTTCGAGAGTATATACCCACCA
ATTCCACCTGCTGTGGCCGCTGTGCATGCTCCCATGCACATGCGAGGCCGCTACCTCGTGG
AGGTGGACCAGGCCTCCTCCAGTGTCTGCCCCCTTCATCATGGACGCACCTCGAGACC
TCAACATTTCTGAGGGTCGGATGGCAGAACTTAAGTGTGCGACTCCCCCTATGTCTCCG
TGAAGTGGTTGCTGCCCAATGGGACAGTGTCTAGCCACGCTCCCGCCACCCAAGGATCT
CTGTCTCAACGACGGCACCTTGAACCTTTCCACGTGCTGCTTTCAGACACTGGGGTGT
ACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCTCGGCCTACCTCAATGTGA
GCACGGCTGAGCTTAACACCTCCAACCTACAGCTTCTTACCACAGTAACAGTGGAGACCA
CGGAGATCTCGCCTGAGGACACAACGCGAAAAGTACAAGCCTGTTCTTACCACGTCCACTG
GTTACCAGCCGGCATATACACCTCTACCACGGTGTCTATTGAGACTACCCGTGTGCCCA
AGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGACAGACCAGCCTGGATGAAG
TCATGAAGACCACCAAGATCATCATTTGGCTGCTTTGTGGCAGTACTCTGCTAGCTGCCG
CCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTCAAG
CCGCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCAGCAGCAACATCCGCAG
CAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGTGCTGCCCAATTC
ATGACCATATTAACCTACAACCTACAACCCAGCACATGGGGCCCACTGGACAGAAAACA
GCCTGGGAACTCTCTGCACCCACAGTCAACCTATCTGAACTTATATAATTGAGA
CCCATAACCAAGGACAAGGTACAGGAACTCAAATA TGACTCCCCTCCCCAAAAAATTA
TAAAATGCAATAGAAATGCACACAAAGACGAACTTTTGTACAGAGTGGGGAGAGACTTT
TTCTGTATATGCTTATATAATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATAA
AATTTAAAGACAAAAGTCAAAACA

FIGURE 30A

DNA58721

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58721
><subunit 1 of 1, 653 aa, 1 stop
><MW: 72717, pI: 6.99, NX(S/T): 10
MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAASAGPQNCPSVCSCSNQFSKVV
CTRRGLSEVPQGI PSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFN
GLASLNTLELFDNWLTVIPSGAFEYLSKLRRLWLRNNPIESIPSYAFNRVPSLMRLDLGE
LKKLEYISEGAFEGFLNFKYLNLMGMCNIKDMPNLTPLVGLLEEMSGNHFFPEIRPGSFRG
LSSLLKLLWVMNSQVSLIERNAFDGLASLVELNLAHNNLSSLPDHLFTPLRYLVELHLHHN
PWNCDCDILWLAFWLREYIPTNSTCCGRCHAPMHRGRYLVEVDQASFQCSAPFIMDAPR
DLNISEGRMAELKCRTPPMSSVKWLLPNGTVLSHASRHPRISVLNDGTLNFSHVLLSDTG
VYTCMVTNVAGNSNAAYLNVSTAE LN TSNYSFFTTVTIVETTEISPEDTTRKYKVPVPTS
TGYQPAYTTSTTVLIQTTRVPKQVAVPATD TTDKMQTSLDEVMKTTKIIIGCFVAVTLLA
AAMLI VFYKLRKRHQQRSTVTAARTVEI IQVDEDIPAATSAAATAAPSGVSGEGAVVLP T
IHDHINYNTYKPAHGAHWTE NSLGN SLHPTVTTISEFYIIQHTTKDKVQETQI
```

Signal sequence.

amino acids 1-41.

Transmembrane domain.

amino acids 12-32, 526-546.

N-glycosylation site.

amino acids 277-280, 322-325, 363-366, 388-391, 410-413, 434-437, 440-443, 447-450, 450-453.

Glycosaminoglycan attachment site.

amino acids 591-594.

Protein kinase C phosphorylation site.

amino acids 62-63, 94-96, 110-112, 243-245, 381-383, 469-471, 470-472, 497-499, 512-514, 525-527, 609-611.

Casein kinase II phosphorylation site.

amino acids 255-258, 267-270, 442-445, 465-468, 517-520, 518-521, 600-603, 633-636.

N-myristoylation site.

amino acids 72-77, 117-122, 190-195, 236-241, 389-394, 420-425, 431-436, 531-536, 615-620.

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 42-52.

FIGURE 30B

Leucine zipper pattern.
amino acids 271-292.

Leucine Rich Repeat.
amino acids 76-99, 100-123, 124-147, 148-171, 172-196, 197-218, 219-242, 243-266, 267-290.

Leucine rich repeat C-terminal domain.
amino acids 300-351.

Leucine rich repeat N-terminal domain.
amino acids 45-74.

FIGURE 31

DNA335924

GCTGAAAGGGCCACGTTTGTTCATTACAAATAAGACCACCGAGTGGGCTCCTGGCGTG
GGGGCGGGAGCAGCCGCGCGCAGTCTTCAGAGGCAGCCCCCAGGCTGTCTCTGGAGGGT
GTGTCTCTGCTTCCCTTTCCCGTGTATTATTTTCAGACGAAGCCAAGTGGCCCGGGGGA
CCCTCCGGACTCCCAGCCTTCAGAGAGGAGGGCAGCTCGGGCTTCGCCGCAGTGTCTCC
TGCCCGTACAGTGTGTGCTCTAGCCGGGGTCCGGGGAGCTGGTATCTTGGCCCTTCTGG
GAGGACGCGCACAGCCGAGGAGGCAGAGCCCCAGACGGGAATGGGCTTTTCAGAGGTGG
GGTGCGGGCGAGGGGACGATGCATTATTTTAAATATTTGATTTATTTTCCAAGTGGACT
TCTTCCCGGGGCTCTTCTGGGCCAGCTGCCTTTGTGATCCCGCGCCCCGGTCTCTGGC
CTCTCACCTCCAGCGCCGGGGCGCCCCCTGCTGTCCGAAGCGGCTGTGACCGGGCAGAGG
TGCTATCTGGGACTCTGGGTTCTCAGCCCAGGGACAGCGAACCGAGGGGCAGATGATCCA
TCAGAAAAGAGCCGGCACTGCCAGCCCCGCGCCCCCTGCCCTGCCTTTTCCGGGAGCG
CGCCGGCCGCACCCGCTACGGCCGCTTGACCCATCTTTGAGCCCGGCCCAAGCTCTG
GGACCGTCGTGCCCTCATCAAGGAAGAGCCAAAGGACCCCAAGGAGAAGGTCAGGAGCGG
CGGTGTGGATGTCCCTTGGCTGCAGGCCCCGCGCGCACTCCCTTCAGTCTTGCCTTCT
CTAGGGACCAGGTAGCATCAGTGCCCTGGATCTCGGCCTTGTTGTGCCCTGCTCCCTGCCCC
ACCTACTAAGAACCAAGTCTGGTTCACCGGCTCCCAAGAGCTGGAACCCATTCTCAGCTA
GCTGGGGGCCAGGCCACCCCTTCCCTCCAGACCTGTGTGCCCTTCTGCCCTGGCTCCAGG
GCCCCCACACCGTGACCAGGGCGGGATCCCTATGGGGCTGGCCAGTCCGCACCGTGCCA
GGCCCCACAGTGCCCTGGGCGTCCATGGAAGTCGTTCTGTGTCTT TAAAATCAGAAGGAAG
ACATTAACCTTTAGGCTGAAGAAAATGTTTTAGTACACAGCAATAACTTATTGTCTTTA
TCCAACAGCCATAAAAATATAACTTTAAATATTCATTGATAGAGAAAGGAGTTCATGAAG
GCAGAAATGCCGCGGCCACGAACATCCAGTGTGGCCCTGGACGGGACATCATGCTGG
GCAACACAGCTAAAATGCGGGTGAAGACCAGATTTCTTGCCATGGCGGTGACGGGATGC
TCCCTAGAGAGCTTCAAGTGGATTCTTTGCTTTTATTTTCTCTTAATAAAAATGTAT
GATGTTACATTGTCAGAGAACAAAAGAAAAA

FIGURE 32

DNA335924

><subunit 1 of 1, 112 aa, 1 stop

><MW: 12158, pI: 11.55, NX(S/T): 0

MSLGCRPRRALPSVLPFSRDQVASVPGSRPCVPCSLPHLLRRTKSGSPAPKSWNPFSASWG
PRPPLPSRPVCLLPWLQGPPhRDQGGIPMGLASRRHRARPTVPWASMEVVLC

N-myristoylation site.

amino acids 27-32, 86-91.

FIGURE 33

DNA340394

ATATATCGATATIGCTGCCGAGGCTGTTGCTGTTGATCTGTGCTCCACTCTGTGAACCTGC
CGAGCTGTTTTTGATAGCCAGCCCCCTCCCATCCCACAGAGGGGAGCCAGTGACCCCTGAC
GTGTAAGATGCCCTTTCTACAGAGTTCAGATGCCAGTTCAGTTCCTGCTTTTTTCAGAGA
CACCCGGGCCTTGGGCCCAGGCTGGAGCAGCTCCCCAAGCTCCAGATCGCTGCCATGTG
GAAAGAAGACACAGGGTCATACTGGTGCAGGCACAGACAATGGCGTCCAAAGTCTTGAG
GAGCAGGAGATCCCAGATAAATGTGCACAGGGTCCCTGTCGCTGATGTGAGCTTGGAGAC
TCAGCCCCCAGGAGGACAGGTGATGGAGGGAGACAGGCTGGTCCCTCATCTGCTCAGTTGC
TATGGGCACAGGAGACATCACCTTCCTTTGGTACAAAGGGGCTGTAGGTTTAAACCTTCA
GTCAAAGACCCAGCGTTCACTGACAGCAGAGTATGAGATTCCCTCAGTGAGGGAGAGTGA
TGCTGAGCAATATTACTGTGTAGCTGAAAATGGCTATGGTCCCAGCCCAGTGGGCTGGT
GAGCATCACTGTGAGAAATCCCGGTGTCGCGCCAATCCTCATGCTCAGGGCTCCCAGGGC
CCAGGCTGCAGTGGAGGATGTGCTGGAGCTTCACTGTGAGGCCCTGAGAGGCTCTCTCC
GATCCTGTACTGGTTTTATCACGAGGATATCACCCCTGGGGAGCAGGTCCGCCCCCTCTGG
AGGAGGAGCCTCCTTCAACCTTTCCCTGACTGAAGAACATTCTGGAAACTACTCCTGTGA
GGCCAACAATGGCCTGGGGGCCAGCGCAGTGGGGGTGACACTCAACTTCACAGTGCC
TACTGGGGCCAGAAGCAATCATCTTACCTCAGGAGTATTGAGGGGCTGCTCAGCACCCCT
TGGTCCAGCCACCGTGGCCTTATTATTTGCTACGGCCTCAAAGAAAAATAGGAAGACG
TTCAGCCAGGGATCCACTCAGGAGCCTTCCCAGCCCTTACCCCAAGAGTTCAGGTACCT
CAACTCACCTACCCAGGGCAGCTACAGCCTATATATGAAAATGTGAATGTTGTAAGTGG
GGATGAGGTTTATTCACTGGCGTACTATAACCAGCCGGAGCAGGAATCAGTAGCAGCAGA
AACCTTGGGGACACATATGGAGGACAAGGTTTCCCTTAGACATCTATTCCAGGCTGAGGAA
AGCAAACATTACAGATGTGGACTATGAAGATGCTATGTAAGGTTATGGAAGATTCTGCTC
TT

FIGURE 34

DNA340394

><subunit 1 of 1, 429 aa, 1 stop

><MW: 46936, pI: 5.42, NX(S/T): 4

MLPRLLLLICAPLCEPAELFLIASPSHPTEGSPVTLTCKMPFLQSSDAQFQFCFFRDTRA
LGPGWSSSPKIQIAAMWKEDTGSYWCEAQTMASKVLRSSRSQINVHRVPVADVLSLETQPP
GGQVMEGDRVLVLCISVAMGTGDITFLWYKGAVGLNLQSKTQRSLTAEYEIPSVRESDAEQ
YYCVAENGYGPPSPGLVSITVRI PVSRPILMLRAPRAQAAVEDVLELHCEALRGSPPILY
WYFHEDITLGSRSAPSGGGASFNLSTEEHSGNYSCEANGLGAQRSEAVTLNFTVPTGA
RSNHLTSGVIEGLLSTLGPATVALLFCYGLKRKIGRRSARDPLRSPLPSLPQEFTYLNSP
TPGQLQPIYENVNVVSGDEVYSLAYYNQPEQESVAAETLGTHMEDKVSLELDIYSRLRKANI
TDVDYEDAM

Signal sequence.

amino acids 1-16.

N-glycosylation site.

amino acids 263-266, 273-276, 293-296, 419-422.

Glycosaminoglycan attachment site.

amino acids 256-259.

Protein kinase C phosphorylation site.

amino acids 37-39, 68-70, 98-100, 160-162, 172-174, 200-202, 338-340.

Casein kinase II phosphorylation site.

amino acids 172-175, 176-179, 265-268, 338-341, 376-379, 401-404, 421-424.

Tyrosine kinase phosphorylation site.

amino acids 174-181.

N-myristoylation site.

amino acids 31-36, 82-87, 257-262, 259-264, 272-277, 283-288, 299-304, 308-313, 312-317.

Amidation site.

amino acids 334-337.

Immunoglobulin.

amino acids 31-88, 127-185, 222-278.

FIGURE 35

DNA56041

GATGTGCTCCTTGGAGCTGGTGTGCAGTGTCTGACTGTAAGATCAAGTCCAAAACCTGTT
TTGGAATTGAGGAACTTCTCTTTTGATCTCAGCCCTTGGTGGTCCAGGTCTTC ATGCTG
CTGTGGGTGATATTACTGGTCTGGCTCCTGTCAGTGGACAGTTTGCAAGGACACCCAGG
CCCATTATTTTCTCCAGCTCCATGGACCACAGTCTTCCAAGGAGAGAGAGTGACCCCTC
ACTTGCAAGGGATTTGCTTCTACTCACACAGAAAACAAAATGGTACCATCGGTACCTT
GGGAAAGAAATACTAAGAGAAACCCAGACAATATCCTTGAGGTTCAGGAATCTGGAGAG
TACAGATGCCAGGCCAGGGCTCCCTCTCAGTAGCCCTGTGCACTTGGATTTTCTTCA
GAGATGGGATTTCTCATGCTGCCAGGCTAATGTTGAACTCCTGGGCTCAAGTGATCTG
CTCACCTAGGCCTCTCAAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTT
TCTGTGTTTGAAGGAGACTCTGTGGTTCTGAGGTGCCGGGCAAAGGCGGAAGTAACACTG
AATAATACTATTTACAAGAATGATAATGTCTGGCATTCTTAATAAAAGAAGTACTTC
CAAAAAAAAAAAAAAAAAAAAAA

FIGURE 36

DNA56041

><subunit 1 of 1, 124 aa, 1 stop

><MW: 14080, pI: 7.48, NX(S/T): 0

MLLWVILLVLPVSGQFARTPRPIIFLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHR
YLGKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLDFSSEMGPAAQANVELLGSS
DLLT

Signal sequence.

amino acids 1-15.

Protein kinase C phosphorylation site.

amino acids 20-22, 43-45.

N-myristoylation site.

amino acids 89-94.

FIGURE 37

DNA59607

GGATTTTGTGATCCGCGATTCCGCTCCACGGGCGGGACCTTTGTAATCGGGGAGGCC
AGGACAGGCCACCCTGCGGGCGGGAGGCAGCCGGGGTGAAGAAACCAAG
ACGAGAGAGGCCAAGCCCCCTGCTTGGGTACACAGCCAAAGGAGGCAGAGCCAGAAC
TCACAACCAGATCCAGAGGCAACAGGGACATGGCCACCTGGGACGAAAAGGCAGTCACCC
GCAGGGCCAAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACCTCACGGTCG
TGGGAGACGACTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGG
AGGAGGAGGAGGAGCAGCCACCACCCACACCAGTCTCAGGCGAGGAAGGCAGAGCTGCAG
CCCCTGACGTTGCCCTGCCCCGCCCCGACCCAGGGCCCCCCTTGACTTCAGGGGCA
TGTTGAGGAACTGTTGAGCTCCACAGGTTTCAGGTCATCATCATCTGCTTGGTGGTTC
TGGATGCCCTCCTGGTGCTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCGAC
AGAAATAACTATGCTGCCATGGTATCCACTACATGAGCATCACCATCTTGGTCTTTTTTA
TGATGGAGATCATCTTTAAATTATTTGTCTTCCGCTGAGTCTTTCACCACAAGTTTGA
GATCCTGGATGCCCGTCGTGGTGGTCTCATTTCATCCTGGACATTTGCTCCTGTTCC
AGGAGCACCAGTTTGAGGCTCTGGCCCTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCC
GGATCATCAATGGGATTATCATCTCAGTTAAGACACGTTTCAAGCGGCAACTCTTAAGGT
TAAAACAGATGAATGTACAATTGGCCGCAAGATTCAACACCTTGAGTTCAGCTGCTCTG
AGAAAGCCCTGGACTGATGAGTTTGTGTATCAACCTGTAAGGAGAAGCTCTCTCCGGAT
GGCTATGGGAATGAAAGAATCCGACTTCTACTCTCACACAGCCACCGTGAAGTCTGGA
GTAAAATGTGCTGTGTACAGAAGAGAGAGAAGGAAGCAGGCTGGCATGTTCACTGGGCTG
GTGTTACGACAGAGAACCTGACAGTCACTGGCCAGTTATCACTTCAGATTACAAATCACA
CAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAACCAAAATCTATAAAGATATTCT
GAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAA

FIGURE 38

DNA59607

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59607

><subunit 1 of 1, 255 aa, 1 stop

><MW: 29405, pI: 7.64, NX(S/T): 0

MATWDEKAVTRRAKVAPAERM SKFLRHFTVVGDDYHAWNIN YKKWENEEEEEEEEQPPPT
PVSGE EGRAAAPDVAPAPGPAPRAPLDFRGM LRKLFSSHRFQV I ICLVVLDALLVLAEL
ILDLK I IQPDKNNYAAMVFHYMSITILVFFMMEIIFKLFV FRLSSFTTSLRSWMPV VVVV
SPILDIVLLFQEHQFEALGLLILLRLWRVARIINGI IISVKTRSERQLLRLKQMNVLAA
KIQHLEFSCSEKPLD

Transmembrane domain.

amino acids 101-121, 141-161, 168-188, 195-215.

Protein kinase C phosphorylation site.

amino acids 20-22, 43-45.

N-myristoylation site.

amino acids 89-94.

FIGURE 39B

AATCTCCCCTGTGCCTGATCTGTGTGTTCCCCAGGAAGAGAGCAGGCAGCCTCTGAGCAA
GCACTGTGTTATTTTCACAGTGGAGACACGTGGCAAGGCAGGAGGGCCCTCAGCTCCTAG
GGCTGTCGAATAGAGGAGGAGAGAGAAATGGTCTAGCCAGGGTTACAAGGGCACAATCAT
GACCATTTGATCCAAGTGTGATCGAAAGCTGTTAATGTGCTCTCTGTATAAACAATTTGC
TCCAATATTTGTTTCCCTTTTTTGTGTGGCTGGTAGTGGCATTGCTGATGTTTTGGTG
TATATGCTGTATCCTTGCTACCATATTGGG

FIGURE 40A

DNA257955

><subunit 1 of 1, 734 aa, 1 stop

><MW: 80856, pI: 6.97, NX(S/T): 8

MLLWLLLLLILTPGREQSGVAPKAVLLLLNPPWSTAFKGEKVALICSSISHSLAQGDYWYH
DEKLLKIKHDKIQITEPGNYQCKTRGSSLSDAVHVEFSPDWLILQALHPVFEQDNVILRC
QKDNKNTHQKVYKDGKQLPNSYNLEKITVNSVSRDNSKYHCTAYRKFYILDIEVTSKP
LNIQVQELFLHPVLRASSSTPIEGSPMTLTCETQLSPQRPDVQLQFSLFRDSQTLGLCWS
RSPRLQIPAMWTEDESGSYWCEVETVTHSIKKRSLRSQIRVQRVPVSNVNLEIRPTGGQLI
EGENMVLI CSVAQSGT VTF SWHKEGRVRS LGRKTQ RSLLAELHVLTVKESDAGRYCAA
DNVHSPILSTWIRVTVRIPVSHPVLTFRAPRAHTVVGDLLELHCESLRGSPPILYRPFYHE
DVTLGNSSAPSGGGASFNLSLTAEHSGNYS CDADNGLGAQHSHGVSLRVTVVSRPVLT
RAPGAQAVVGDLELHCESLRGSPPILYWFYHEDDTLGNISAHSGGGASFNLSLTTEHSG
NYSCEADNGLGAQHSKVVTLNVTGT SRNR TGLTAAGITGLVLSILVLA AAAALLHYARAR
RKP GGLSATGTSSHS PSECQEPSSSRPSRIDPQEP THSKPLAPMELEPMYSNVNPGDSNP
IYSQIWSIQHTKENSANC PMMHQEHBELTVLYSELKKT HPDDSAGEASSR GRAHEEDDEE
NYENVPRVLLASDH

Signal sequence.

amino acids 1-13.

Transmembrane domain.

amino acids 574-594.

N-glycosylation site.amino acids 426-429, 438-441, 448-451, 519-522, 531-534, 541-544, 561-564,
568-571.**Glycosaminoglycan attachment site.**

amino acids 431-434, 524-527.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 270-273.

Protein kinase C phosphorylation site.amino acids 177-179, 242-244, 268-270, 273-275, 335-337, 347-349, 375-377,
386-388, 406-408, 466-468, 479-481, 499-501, 565-567, 624-626, 708-710.**Casein kinase II phosphorylation site.**

amino acids 88-91, 200-203, 347-350, 615-618, 628-631, 698-701, 703-706.

Tyrosine kinase phosphorylation site.

amino acids 349-356.

FIGURE 40B

N-myristoylation site.

amino acids 78-83, 86-91, 204-209, 236-241, 256-261, 432-437, 434-439, 447-452, 458-463, 518-523, 525-530, 527-532, 540-545, 551-556, 564-569, 571-576, 579-584, 604-609, 605-610.

Amidation site.

amino acids 331-334.

N-6 Adenine-specific DNA methylases signature.

amino acids 25-31.

Immunoglobulin domain.

amino acids 37-84, 113-165, 204-262, 302-360, 397-453, 490-546.

FIGURE 41A

DNA329863

CTCAATCAGCTTTATGCAGAGAAGAAGCTTACTGAGCTCACTGCTGGTGTGGTGTAGGC
AAGTGTGCTTTGGCAATCTGGGCTGACCTGGCTTGTCTCCTCAGAACTCCTTCTCCAAC
CCTGGAGCAGGCTTCCATGCTGCTGTGGGCGTCCCTGGCTGGCCTTTGCTCCAGTCTGTGG
ACAATCTGCAGCTGCACACAAACCTGTGATTTCCGTCCATCCTCCATGGACCACATTCTT
CAAAGGAGAGAGAGTACTCTGACTTGCAATGGATTTCAGTTCTATGCAACAGAGAAAAC
AACATGGTATCATCGGCCTACTGGGGAGAAAAGTTGACCCCTGACCCCAAGAAACCCCT
CGAGGTTCCGGAATCTGGACTGTACAGATGCCAGGCCCGGGGCTCCCCACGAAGTACC
TGTGCGCTTGCTCTTTCTCAGACTCCTTAATCCTGACGGCACCATATTCTGTGTGGA
AGGTGACACATTGGTTCAGATGCCACAGAAGAAGGAAAAGAAAATTGACTGCTGTGAA
ATATACTTGGAAATGAAACATTTCTTTCCATTTCTAATAAAAGCTGGGATCTTCTTATCC
ACAAGCAAGTTCAAATAACAATGGCAATTATCGATGCATGGATATGGAGATGAGAAATGA
TGTATTTAGATCAAATTTCAAATAAATTAATAATCAAGAACTATTTCCACATCCAGAGCT
GAAAGCTACAGACTCTCAGCTACAGAGGGGAATTCTGTAACCTGAGCTGTGAAACACA
GCTTCTCCAGAGCGGTGACACACCCCACTTCACTTCAACTTCTTCAGAGATGGCGAGGT
CATCTGTGACTGGAGCACGTACCCGGAACTCCAGCTCCCAACCGTCTGGAGAGAAA
CTCAGGATCCTATTGGTGTGGTCTGAAACAGTGAGGGGTAACATCCACAAGCACAGTCC
CTCGCTACAGATCCATGTGCAGCGGATCCCTGTGTCTGGGGTCTCCTGGAGACCCAGCC
CTCAGGGGGCCAGGCTGTGAAAGGGAGATGCTGGTCTTGTCTGCTCCGTGGCTGAAGG
CACAGGGGATACACATTTCTCTGGCACCGAGAGGACATGCAGGAGAGTCTGGGGAGGAA
AACTCAGCGTTCCCTGAGAGCAGAGCTGGAGCTCCCTGCCATCAGACAGAGCCATGCAGG
GGGATACTACTGTACAGCAGACAAACAGCTACGGCCCTGTCCAGAGCATGGTGTGAATGT
CACTGTGAGAGAGACCCCAAGCAACAGAGATGGCCTTGTGCGCCGGGAGCCACTGGAGG
GCTGCTCAGTCTCTTCTCCTGGCTGTGGCCCTGCTGTTCACTGCTGGCGTCGGAGGAA
GTCAGGAGTTGGTTCTTGGGAGACGAAACCAGGCTCCCTCCCGCTCCAGGCCAGGAGA
GTCCCTCCATTCATCTGCCCTGCCAGGTGGAGCTTCACTCGTTGTATGTGTATGTACA
CCCCAAAAGGGAGATTTGGTATACTCTGAGATCCAGACTACTCAGCTGGGAGAGAAGA
GGAAAGCTAATACCTCCAGGACACTTCTAGAGGATAAGGATGTCAGTTGTCTACTCTGA
GGTAAAGACACAACCCAGATAACTCAGCTGGAAAGATCAGCTCTAAGGATGAAGAAAG
TTAAGAGAATGAAAAGTTACGGGAACGTCCTACTCATGTGATTTCTCCCTGTCCAAAGT
CCCAGGCCAGTGCAGTCCCTGCGGCACCTGGAATGATCAACTCATTCCAGCTTTCTAAT
TCTTCTCATGCATATGCATTCCTCCAGGAATACTCATTCGTCTACTCTGATGTTGGGA
TGGAATGGCCTCTGAAAGACTTCACTAAAAAGACCAGGATCCACAGTTAAGAGAAGACCC
TGTAATATTGCTGTGGGCTGACCTAATGCATTCCTAGGGTCTGCTTTAGAGAAGGGG
GATAAAGAGAGAGAAGGACTGTTATGAAAAACAGAAGCACAATTTGGTGAATTGGGAT
TTGCAGAGATGAAAAGACTGGGTGACCTGGATCTCTGCTTAATACATCTACAACCATG
TCTCACTGGAGACTCACTTGCATCAGTTTGTGTTAACTGTGAGTGGCTGCACAGGCCTGT
GCAACAATGAAAAGCCCCCTCACTTCTGCTGCACAGCTTACACTGTGAGGATTCAGTT
GCAGATTAAGAACCATCTGGAATGGTTTACAGAGAGAGGAATTTAAAAGAGGACATCA
GAAGAGCTGGAGATGCAAGCTTAGGCTGCGCTTCCAAAAGCAAATGATAATTATGTTAA
TGTCAATAGTGACAAAGATTTGCAACATTAGAGAAAAGAGACACAAATATAAAATTA
AACTTAAGTACCAACTCTCCAAAATAAATTTGAACTTAAAATATTAGTATAAACTCATAA
TAAACTCTGCCTTTAAAAAAGATAAATATTTCTACGCTGTTCCTGAAATAAATACC
AACCCCTTAGCAATAAGCACTCCTTGCAGAGAGGTTTTATTCTCTAATAACCATTCCTT

FIGURE 41B

CTCAAAGGAAATAAGGTTGCTTTTCTTGTAGGAACTGIGTCTTTGAGTTACTAATTAGTT
TATATGAGAATAAATCTTGCAATAAATGAAGAAGGAATAAAAGAAATAGGAAGCCACAAA
TTTGTATGGATATTTTCATGATACACCTACTGGTTAAATAATTGACAAAAACCAGCAGCCA
AATATTAGAGGTCCTCTGATGGAAGTGTACAATACCACCTACAAATTATCCATGCCCCAA
GTGTTAAACTGAATCCATTCAAGTCTTTCTAACTGAATACTTGTTTTATAGAAAATGCA
TGGAGAAAAGGAATTTGTTTAAATAACATTATGGGATTGCAACAGCAAAACATAAACTG
AGAAAAGTTCTATAGGGCAAATCACCTGGCTTCTATAACAAATAAATGGGAAAAAATG
AAATAAAAAGAAGAGAGGGAGGAAGAAAGGGAGAGAGAAGAAAAGAAAATGAAGAAAAG
TAATTAGAATATTTTCAACATAAAGAAAAGACGAATATTTAAGGTGACAGATATCCCAAC
TACGCTGATTTGATCTTTACAAATTATATGAGTGTATGAATTTGTCACATGTATCACCCC
CAAAAAAGAGAAAAAGAAAATAGAAGACATATAAATTAATGAGACGAGACATGTCGA
CCAAAAGGAATGTGTGGGTCTTGTTTGGATCCTGACTCAAATTAAGAAAAATAAACTA
CCTACGAAATACTAAGAAAAATTTGTATACTAATATTAAGAAATGTTTGTGTGTTTTGGA
TATAAGTGATAGTTTATTGTAGTGTATGTTTTTATAAAAGCAAAGGATATTCACTTTCAG
CGCTTATACTGAAGTATTAGATTAAGCTTATTAACGTA

FIGURE 42A

DNA329863

><subunit 1 of 1, 515 aa, 1 stop

><MW: 57224, pI: 6.45, NX(S/T): 4

MLLWASLLAFAPVCGQSAAAHKPVISVHPPWTTFFKGERVTLTCNGFQFYATEKTTWYHR
HYWGEKLTLPNTLEVRRESGLYRCQARGSPRSNPVRLLFSSDSLILQAPYSVFEGDTLV
LRCHRRRKEKLTAVKYTWNGNILSISNKSWDLLIPQASSNNNGNYRCIGYGDENDVFRSN
FKI IKIQELFPPPELKATDSQPTEGNSVNLSCETQLPPERSDTPLHFNFFRDGEVILSDW
STYPELQLPTVWRENSGSYWC GAETVRGNIHKHSPSLQIHVQRI PVSGV LLETQPSSGGQA
VEGEMLVLVCSVAEGTGDTTFSWHREDMQESLGRKTQ RSLRAE LELPAIRQSHAGGYCT
ADNSYGPVQSMVLNVTVRET PGNRDGLVAAGATGGLLSALLLAVALLFHCWRRRKSGVGF
LGDETRLP PAPP GP GESSHSICPAQVELQSLYVDVHPKKGDLVYSEIQTTQLGEEEEANTS
RTLLEDKDVSVVYSEVKTQHPD NSAGKISSKDEES

Signal Sequence.

amino acids 1-16.

Transmembrane domain.

amino acids 387-407.

N-glycosylation site.

amino acids 147-150, 209-212, 374-377, 478-481.

Glycosaminoglycan attachment site.

amino acids 416-419.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 413-416.

Protein kinase C phosphorylation site.

amino acids 52-54, 90-92, 146-148, 265-267, 336-338, 339-341, 376-378, 479-481, 509-511.

Casein kinase II phosphorylation site.

amino acids 112-115, 242-245, 311-314, 376-379, 482-485, 509-512, 510-513.

Tyrosine kinase phosphorylation site.

amino acids 457-463.

N-myristoylation site.

amino acids 15-20, 81-86, 89-94, 140-145, 163-168, 205-210, 257-262, 315-320, 355-360, 382-387, 386-391, 391-396, 394-399, 395-400.

Amidation site.

amino acids 332-335.

FIGURE 42B

Immunoglobulin domain.

amino acids 37-87, 116-169, 205-263, 303-361.

FIGURE 43

DNA346528

ACACACCCACAGGACCTGCAGCTGAACGAAGTTGAAGACAACCTCAGGAGATCTGTTGGAA
AGAGAACGATAGAGGAAAATATATGAATGTTGCCATCTTTAGTTCCTGTGTTGGGAAA
CTGTCTGGCTGTACCTCCAAGCCTGGCCAAACCCTGTGTTTGAAGGAGATGCCCTGACTC
TGGCATGTCAGGGATGGAAGAATACACCACTGTCTCAGGTGAAGTTCACAGAGATGGAA
AATTCCTTCATTTCTAAGGAAAAACAGACTCTGTCCATGGGAGCAGCAACAGTGCAGA
GCCGTGGCCAGTACAGCTGCTCTGGCCAGGTGATGTATATTCACAGACATTCACACAAA
CTTCAGAGACTGCCATGGTTCAGTCCAAGAGCTGTTTCCACCTCCTGTGCTGAGTGCCA
TCCCCCTCCTGAGCCCCGAGAGGGTAGCCTGGTGACCCTGAGATGTCAGACAAAGCTGC
ACCCCTGAGGTCAGCCTTGAGGCTCCTTTTCTCCTTCCACAAGGACGGCCACACCTTGC
AGGACAGGGGCCCTCACCCAGAACTCTGCATCCCGGGAGCCAAGGAGGGAGACTCTGGGC
TTTACTGGTGTGAGGTGGCCCTGAGGGTGGCCAGGTCCAGAAGCAGAGCCCCCAGCTGG
AGGTGAGAGTGCAGGCTCCTGTATCCCGTCTGTGCTCACTCTGCACCACGGGCCTGCTG
ACCCTGTGTGGGGACATGGTGCAGCTCCTCTGTGAGGCACAGAGGGGCTCCCCCTCCGA
TCCTGTATTCCTTCTACCTTGATGAGAAGATTGTGGGAACCACTCAGCTCCCTGTGGTG
GAACCACCTCCCTCTCTCCAGTGAAGTCAGAACAGGATGCTGGGAACACTCTCTGCGG
AGGCTGAGAACAGTGTCTCCAGAGAGAGGAGTGAGCCCAAGAAGCTGTCTCTGAAGGGTT
CTCAAGTCTTGTTCACTCCCGCCAGCAACTGGCTGGTTCCTTGGCTTCCCTGCGAGCCTGC
TTGGCCTGATGGTTATTGCTGCTGCACCTCTGGTTTATGTGAGATCCTGGAGAAAAGCTG
GGCCCTTCCATCCGAGATACCACCCACAGCTCCAGGTGGAGAGCAGTGCCTACTATATG
CCAACGTGCATCACAGAAAGGGAAAGATGAAGGTGTTGTC TACTCTGTGGTGCATAGAA
CCTCAAAGAGGAGTGAAGGACAGTTCATCATCTGTGCGGAGGTGAGATGCCTGCAGCCC
AGTGAGGTTTCATCCACGGAGGTGAATATGAGAAGCAGGACTCTCCAAGAACCCTTAGC
GACTGTGAGGAGGTTCTCTGCTAGTGTGATGGTGTCTCCTATCAACACACGCCACCCCCA
GTCTCCAGTGTCTCCTCAGGAAGACAGTGGGGTCTCAAATCTTTCTGTGGGTCCCTCAGT
TCCCAAGCCCAGCATCACAGAGCCCCCTGAGCCCTGTCTGCTCAGGAGCACCTGAACC
CTGGGTTCTTTCTTAGCAGAAGACCAACCAATGGAATGGGAAGGGAGATGCTCCACCA
ACACACACACTTAGGTTCAATCAGTGACACTGGACACATAAGCCACAGATGTCTTCTTTC
CATAAAGCATGTTAGTTCGCCCAATATACATATATATATGAAATAGTCATGTGCCGCA
TAACAACATTTAGTCACTGATAGACTGCATACACAACAGTGGTCCATAAGACTGTAAT
GGAGTTTAAAAAATTCCTACTGCTAGTATATCATAGTTCCTTAAACATCATAACACAAC
ACATTTCTCACGCTTTGTGGTGTGCTGGTACAAACAAGCTACAGCGCCGCTAGTCATA
TACAAATATAGCACATACAATTATGTACAGTACACTATACTTGATAATGATAATAAACAA
CTATGTTACTGGT

FIGURE 44

DNA346528

><subunit 1 of 1, 392 aa, 1 stop

><MW: 42948, pI: 8.37, NX(S/T): 3

MLPSLVPCVGTKTVWLYLQAWPNPVFEGDALTLRCQGWKNTPLSQVKFYRDGKFLHFSKEN
QTLSMGAATVQSRGQYSCSGQVMYIPQTFOTSETAMVQVQELPPPPVLSAIPSEPEPREG
SLVTLRCQTKLHPLRSALRLLFSFHKDGHTLQDRGPHPELCIPGAKEGDSGLYWCEVAPE
GGQVQKQSEPLEVRVQAPVSRPVLTLHHGPADPAVGDMVQLLCEAQRGSPPILYSFYLDE
KIVGNHSAPCGGTTSLFFVKSEQDAGNYSCEAENSVSRERSEPKKLSLKGSQVLFTPAS
NWLVPWLPASLLGLMVIAAALLVYVRSWRKAGPLPSQIPPTAPGGEQCPLYANVHHQKKGK
DEGVVYSVVHRTSKRSEGGFYHLCCGEMPAAQ

Transmembrane domain.

amino acids 302-322.

N-glycosylation site.

amino acids 60-63, 245-248, 268-271.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 285-288.

Protein kinase C phosphorylation site.

amino acids 31-33, 124-126, 288-290, 327-329, 372-374, 373-375.

Casein kinase II phosphorylation site.

amino acids 150-153, 262-265.

Tyrosine kinase phosphorylation site.

amino acids 166-173, 261-269, 358-366, 374-381.

N-myristoylation site.

amino acids 74-79, 120-125, 164-169, 171-176, 251-256, 267-272, 363-368.

Immunoglobulin domain.

amino acids 27-80, 120-177, 216-273.

FIGURE 45

DNA212930

CCATTGTTCTCAACATTCTAGCTGCTCTTGCTGCATTGCTCTGGAATTCCTGTAGAGAT
ATTACTTGTCCCTCCAGGCTGTTCTTTCTGTAGCTCCCTTGTTTTCTTTTGTGATC ATG
TTGCAGATGGCTGGGCAGTGC TCCCAAAATGAATATTTGACAGTTTGTTCATGCTTGC
ATACCTTGTCAACTTCGATGTTCTTCTAATACTCCTCCTCTAACATGTCAGCGTTATTG'
AATGCAAGTGTGACCAATTCAGTCAAAGGAACGAATGCGATTCTCTGGACCTGTTTGGGA
CTGAGCTTAATAATTTCTTTGGCAGTTTTCTGTCTAATGTTTTTGCTAAGGAAGATAAGC
TCTGAACCATTAAGGACGAGTTTAAAAACACAGGATCAGGTCTCCTGGGCATGGCTAAC
ATTGACCTGGAAAAGAGCAGGACTGGTGATGAAATTATTCTCCGAGAGGCCTCGAGTAC
ACGGTGAAGAATGCACCTGTGAAGACTGCATCAAGAGCAAACCGAAGGTGACTCTGAC
CATTGCTTTCCACTCCAGCTATGGAGGAAGGCGCAACCAATCTTGTACCACGAAAACG
AATGACTATTGCAAGAGCCTGCCAGCTGCTTTGAGTGCTACGGAGATAGAGAAATCAATT
TCTGCTAGGTAATTAACCATTCGACTCGAGCAGTGCCACTTTAAAAATCTTTTGTGAGA
ATAGATGATGTGTCAGATCTCTTTAGGATGACTGTATTTTTTCAATTGCCGATACAGCTTT
TTGTCCCTCTAACTGTGGAAACTCTTTATGTTAGATATATTTCTCTAGGTTACTGTTGGGA
GCTTAATGGTAGAAACTTCCTTGGTTTTCATGATTAAAGTCTTTTTTTTTCTTGAAAAAAA

FIGURE 46

DNA212930

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA212930

><subunit 1 of 1, 184 aa, 1 stop

><MW: 20138, pI: 5.30, NX(S/T): 1

MLQMAGQCSQNEYFDSLHACIPCQLRCSNTTPPLTCQRYCNASVTNSVKGTNAILWTCL
GLSLIISLAVFVLMFLLRKISSEPLKDEFKNTGSGLLGMANIDLEKSRTGDEILPRGLE
YTVVEECTCEDCIKSKPKVDSHDHCFPLPAMEEGATILVTTKTNDYCKSLPAALSATEIEKS
ISAR**Signal sequence.**

amino acids 1-28.

Transmembrane domain.

amino acids 55-75.

N-glycosylation site.

amino acids 42-45.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 78-81.

Protein kinase C phosphorylation site.

amino acids 48-50, 158-160, 182-184.

Casein kinase II phosphorylation site.

amino acids 9-12, 109-112, 122-125, 127-130, 173-176, 175-178.

N-myristoylation site.

amino acids 118-123.

FIGURE 47

DNA335918

CTTCCCAGCCTTCGGAACCTATGGAGCCCGCACTCTCCAGTTCATCACCACCCAGCATCC
CTACTCTTGCATCTAACAGTTTCCGCTATTTTGCACCACCTGCCINGNCCTTATGGGCAA
CTCAAGGAAGAAAGGAAAGAAGAGATAGAGGAAAAATGGATTCAACANATGAAAGTGTC
TTTCTGACTACTGCTGTGTTACAAACATTTTAATCATCAAACATGCTTTATTTGATAG
AAAGATCAAATCTGCCTTTGTAAAACAAGAGACTATTTTAATCATTAAGACAACACANAT
GTTTGATTGGAGGCGTGTCTCATTCAAACCTTGC

FIGURE 48

DNA225820

GGAGAGTCTGACCACCATGCCACCTCCTCGCCTCCTCTTCTTCCCTCCTCTTCTCACC
CATGGAAGTCAGGCCCGAGGAACCTCTAGTGGTGAAGGTGGAAGAGGGAGATAACGCTGT
GCTGCAGTGCCTCAAGGGGACCTCAGATGGCCCCACTCAGCAGCTGACCTGGTCTCGGGA
GTCCCCGCTTAAACCTTCTTAAACTCAGCCTGGGGCTGCCAGGCCTGGGAATCCACAT
GAGGCCCTGGCCATCTGGCTTTTTCATCTTCAACGCTCTCTCAACAGATGGGGGGCTTCTA
CCTGTGCCAGCCGGGGCCCCCTCTGAGAAGGCCTGGCAGCCTGGCTGGACAGTCAATGT
GGAGGGCAGCGGGAGCTGTTCCGGTGAATGTTTCGGACCTAGGTGGCCTGGGCTGTGG
CCTGAAGAACAGGTCCCTCAGAGGGCCCCAGCTCCCCTCCGGGAAGCTCATGAGCCCCAA
GCTGTATGTGTGGGCCAAAGACCGCCCTGAGATCTGGGAGGGAGAGCCTCCGTGTGTCCC
ACCGAGGCACAGCCTGAACCAGAGCCTCAGCCAGGACCTCACCATGGCCCCCTGGCTCCAC
ACTCTGGCTGTCTGTGGGGTACCCCCGACTCTGTGTCCAGGGGCCCTCTCCTGGAC
CCATGTGCACCCCAAGGGCCCTAAGTCATTGCTGAGCCTAGAGCTGAAGGACGATCGCC
GGCCAGAGATATGTGGTAAATGGAGACGGGTCTGTTGTGCCCCGGGCCACAGCTCAAGA
CGCTGGAAAGTATTATTGTCACCGTGGCAACCTGACCATGTCAATCCACCTGGAGATCAC
TGCTCGGCCAGTACTATGGCACTGGCTGCTGAGGACTGGTGGCTGGAAGGTCTCAGTGT
GACTTTGGCTTATCTGATCTTCTGCCTGTGTCCCTTGTGGGCATTTCTTCTTCAAAG
AGCCCTGGTCTTGAGGAGGAAAAGAAAGCGAATGACTGACCCACCCAGGAGATTCTTCAA
AGTGACGCCCTCCCCAGGAAGCGGGCCCCAGAACAGTACGGGAACGTGCTGTCTCTCCC
CACCCACCTCAGGCCTCGGACCGGCCAGCGTTGGGCCGAGGCCTGGGGGGCACTGC
CCCGTCTTATGGAAACCCGAGCAGCGACGTCCAGGCGGATGGAGCCTTGGGGTCCCCGAG
CCGCCGGGAGTGGGCCCAGAAGAAGAGGAAGGGGAGGGCTATGAGGAACCTGACAGTGAG
GAGGACTCCGAGTTCTATGAGAACGACTCCAACCTTGGGCAGGACCAGCTCTCCAGGAT
GGCAGCGGCTACGAGAACCCTGAGGATGAGCCCCTGGGTCTGAGGATGAAGACTCCTTC
TCCAACGCTGAGTCTTATGAGAACGAGGATGAAGAGCTGACCCAGCCGGTCCGACAGGACA
ATGGACTTCCTGAGCCCTCATGGGTGAGCCTGGGACCCAGCCGGGAAGCAACCTCCCTG
GGGTCCCAGTCCATGAGGATATGAGAGGAATCCTGTATGCAGCCCCCAGCTCCGCTCC
ATTCCGGGCCAGCCTGGACCCAATCATGAGGAAGATGCAGACTCTTATGAGAACATGGAT
AATCCCGATGGGCCAGACCCAGCCTGGGGAGGAGGGGGCCGCATGGGCACCTGGAGCACC
AGGTGATCCTCAGGTGGCCAGCCTGGATCTCCTCAAGTCCCCAAGATTCACACCTGACTC
TGAAATCTGAAGACCTCGAGCAGATGATGCCAACCTCTGGAGCAATGTTGCTTAGGATGT
GTGCATGTGTGTAAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTATACATGCCAGT
GACACTCCAGTCCCCCTTGTATTCCTTAAATAAACTCAATGAGCTCTTCAAAAAAAAAA
AA

FIGURE 49A

DNA225820

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA225820
><subunit 1 of 1, 467 aa, 1 stop
><MW: 51818, pI: 10.69, NX(S/T): 7
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MPPPRLLFFLLFLTPMEVRPEEPLVVKVEEGDNAVLQCLKGTSDGPTQQLTWSRESPLKP
FLKLSLGLPGLGIHMRPLAIWLFIFNVSQQMGGFYLCQPGPPSEKAWQPGWTVNVEGSGE
LFRWNVSDLGGLGCGLKNRSSEGPSSPSGKLMSPKLYVWAKDRPEIWEGEPPFCVPPRDSL
NQSLSQDLTMAPGSTLWLSGVPDPSVSRGPLSWTHVHPKGPKLLSLELKDDRPARDMW
VMEtGLLLPRATAQDAGKYYCHRGMLTMSFHLEITARFVLWHWLLRTGGWKVSAVTLAYL
IFCLCSLVGILHLQRALVLRKRKRMTDPTRRFKVTPPFGSGPQNOYGNVLSLPTPTSG
LGRAQRWAAGLGGTAPSYGNPSSDVQADGALGSRSRREWAQKKRGRAMRNLTVRRTPSS
MRTTPTLGRtSSPRMAAATRTLRLMSPWVLRMKTSPSTLSLMRTRMKs
```

Signal Sequence.

Amino acids 1-20.

Transmembrane Domain.

Amino acids 294-314.

Immunoglobulin Domain.

Amino acids 31-99, 193-263.

N-glycosylation Site.

Amino acids 86-89, 125-128, 138-141, 181-184, 265-268, 411-414.

Glycosaminoglycan attachment site.

Amino acids 359-362.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 324-327.

Protein kinase C phosphorylation site.

Amino acids 103-105, 148-150, 153-155, 275-277, 330-332, 395-397, 413-415, 420-422, 432-434, 441-443.

Casein kinase II phosphorylation site.

Amino acids 14-17, 252-255, 395-398.

Figure 49B

N-myristoylation Site.

Amino acids 130-135, 131-136, 349-354, 360-365, 370-375, 373-378, 379-384, 389-394.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 190-200.

FIGURE 50A

DNA88116

CCATCCCATAGTGAGGGAAGACACGCGGAAACAGGCTTGCACCCAGACACGACACCATGC
ATCTCCTCGGCCCTGGCTCCTGCTCCTGGTTCTAGAATACTTGGCTTCTCTGACTCAA
GTAAATGGGTTTTTTGAGCACCTGAAACCTCTACGCCTGGGAGGGGGCCTGCGTCTGGA
TCCCCTGCACCTACAGAGCCCTAGATGGTGACCTGGAAAGCTTCATCCTGTTCACAATC
CTGAGTATAACAAGAACACCTCGAAGTTTGATGGGACAAGACTCTATGAAAGCACAAAGG
ATGGGAAGGTTCTTCTGAGCAGAAAAGGGTGCAATCCTGGGAGACAAGAATAAGAACT
GCACACTGAGTATCCACCCGGTGCACCTCAATGACAGTGGTCAGCTGGGGCTGAGGATGG
AGTCCAAGACTGAGAAATGGATGGAACGAATACACCTCAATGTCTCTGAAAGGCCTTTTTC
CACCTCATATCCAGCTCCCCTCCAGAAATCAAGAGTCCCAGGAAGTCACTCTGACCTGCT
TGCTGAATTTCTCCTGCTATGGGTATCCGATCCAATTGCAGTGGCTCCTAGAGGGGGTTC
CAATGAGGCAGGCTGCTGTACCTCGACCTCCTTGACCATCAAGTCTGTCTTCACCCGGA
GCGAGCTCAAGTTCTCCCCACAGTGGAGTCACCATGGGAAGATTGTGACCTGCCAGCTTC
AGGATGCAGATGGGAAGTTCCTCTCCAATGACACGGTGCAGCTGAACGTGAAGCACACCC
CGAAGTTGGAGATCAAGGTCACTCCCAGTGTGCCATAGTGAGGGAGGGGGACTCTGTGA
CCATGACCTGCGAGGTCAGCAGCAGCAACCCGGAGTACACGACGGTATCCTGGCTCAAGG
ATGGGACCTCGCTGAAGAAGCAGAATACATTACGCTAAACCTGCGCGAAGTGACCAAGG
ACCAGAGTGGGAAGTACTGCTGT CAGGTCTCCAATGACGTGGGCCCGGGAAGGTCGGAAG
AAGTGTTCCTGCAAGTGCAGTATGCCCGGAACCTTCCACGGTTCAGATCCTCCACTCAC
CGGCTGTGGAGGGAAGTCAAGTFCAGTTTTCTTTGCATGTCACTGGCCAATCCTCTTCCAA
CAAATTACAGTGGTACCACAATGGGAAAGAAATGCAGGGAAGGACAGAGGAGAAAGTCC
ACATCCCAAAGATCCTCCCCTGGCACGCTGGGACTTATTCCTGTGTGGCAGAAAACATTCT
TTGGTACTGGACAGAGGGGGCCCGGAGCTGAGCTGGATGTCCAGTATCCTCCAAAGAGG
TGACCACAGTGATTCAAACCCCATGCCGATTCGAGAAGGAGACACAGTGACCCTTTCTCT
GTAACTACAATTCCAGTAACCCAGTGTACCCCGGTATGAATGGAAACCCCATGGCGCCT
GGGAGGAGCCATCGCTTGGGGTGTGTAAGATCCAAAACGTTGGCTGGGACAACACAACCA
TCGCCTGCGCACGTTGTAATAGTTGGTGTCTCGTGGGCCTCCCCTGTGCGCCTGAATGTCC
AGTATGCCCCCGAGACGTGAGGGTCCGGAAAATCAAGCCCTTTCCGAGATTCACTCTG
GAAACTCGGT CAGCCTCCAATGTGACTTCTCAAGCAGCCACCCCAAAGAAGTCCAGTTCT
TCTGGGAGAAAAATGGCAGGCTTCTGGGGAAAGAAAGCCAGCTGAATTTGACTCCATCT
CCCCAGAAGATGCTGGGAGTTACAGCTGCTGGGTGAACAACTCCATAGGACAGACAGCGT
CCAAGGCCCTGGACACTTGAAGTGTGTATGCACCCAGGAGGCTGCGTGTGTCCATGAGCC
CGGGGACCAAGTGTGAGGGGAAGAGTGCAACCCTGACCTGTGAGAGTGACGCCAACC
CTCCCGTCTCCACTACACCTGGTTTGACTGGAATAACCAAAGCCTCCCCACCACAGCC
AGAAGCTGAGATTGGAGCCGGTGAAGGTCCAGCACTCGGGTGCCTACTGGTGCCAGGGGA
CCAACAGTGTGGGCAAGGCCGTTTCGCTCTCAGCACCCCTTACTGTCTACTATAGCCCGG
AGACCATCGGCAGGCGAGTGGCTGTGGGACTCGGGTCTCGCCTCGCCATCCTCATCTGG
CAATCTGTGGGCTCAAGCTCCAGCGACGTTGGAAGAGGACACAGAGCCAGCAGGGGCTTC
AGGAGAATTCCAGCGGCCAGAGCTTCTTTGTGAGGAATAAAAAGGTTAGAAGGGCCCCC
TCTCTGAAGGCCCCACTCCCTGGGATGCTACAATCCAATGATGGAAGATGGCATTAGCT
ACACCACCTGCGCTTCCCCGAGATGAACATAACCACGAACTGGAGATGCAGAGTCCCTCAG
AGATGCAGAGACCTCCCCGACCTGCGATGACACGGTCACTTATTTCAGCATTGCACAAGC

FIGURE 50B

GCCAAGTGGGCGACTATGAGAACGTCATTCCAGATTTTCCAGAAGATGAGGGGATTCATT
ACTCAGAGCTGATCCAGTTTGGGGTCGGGGAGCGGCCTCAGGCACAAGAAAATGTGGACT
ATGTGATCCTCAAACATTGACACTGGATGGGCTGCAGCAGAGGCACTGGGGGCAGCGGGG
GCCAGGGAAGTCCCCGAGTTTCCCAGACACCGCCACATGGCTTCCTCCTGCGTGATGT
GCGCACACACACACACACGACACACACACACACACTCACTGCGGAGAACCCTTGTG
CCTGGCTCAGAGCCAGTCTTTTTGGTGAGGGTAACCCCAAACCTCCAAAACCTCCTGCCCC
TGTTCTCTTCCACTCTCCTTGCTACCCAGAAATCATCTAAATACCTGCCCTGACATGCAC
ACCTCCCCTGCCCCACCAGCCCCTGGCCATCTCCACCCGGAGCTGCTGTGTCTCTGGA
TCTGCTCGTCATTTCCCTCCCTTCTCCATCTCTCTGGCCCTCTACCCCTGATCTGACAT
CCCCTCAGCAATATTATGCCAGTTTCTGCCCTCTGAGGGAAAGCCAGAAAAGGACAG
AAACGAAGTAGAAAGGGGCCAGTCTTGGCCTGGCTTCTCCTTTGGAAGTGAGGCATTGC
ACGGGGAGACGTACGTATCAGCGGCCCTTGACTCTGGGACTCCGGTTTGAGATGGAC
ACACTGGTGTGGATTAACCTGCCAGGGAGACAGAGCTCACAAATAAAAATGGCTCAGATGC
CACTTCAAAGAAAAAAAAA

FIGURE 51A

></usr/seqdb2/bst/DNA/Dnaseqs.min/ss.DNA88116
><subunit 1 of 1, 847 aa, 1 stop
><MW: 95452, pI: 6.82, NX(S/T): 13

MHLLGFWLLLLLVLEYLAFSDSSKWFVPEHPETLYAWEGACVWIPCTYRALDGDLESFILFH
NPEYNKNTSKFDGTRLYESTKDGKVPSEQKRVQFLGDKNKNTLSIHPVHLNDSGQLGLR
MESKTEKWMERIHLNVSERFPFPHIQLPPEIQESQEVTLTCLLNFSYGYPIQLQWLLEG
VPMRQAAVTSTSLTIKSVFTRSELKFSQPQWSHHGKIVTCQLQDADGKFLSNDTVQLNVKH
TPKLEIKVTPSDAIVREGDSVTMTCEVSSSNPEYTTVSWLKDGTSLKKQNTFTLNLREVT
KDQSGKYCCQVSNVGVGPRSEEVFLQVQYAPEPSTVQILHSPAVEGSQVEFLCMSLANPL
PTNYTWYHNGKEMQGRTEEKVHI PKILPWHAGTYSCVAENILGTGQRGPGAELDVQYPPK
KVTTVIQNPMPIREGDVTVLSNYSNPNPSVTRYEWKPHGAWPEPSLVGLKIQNVGWDNT
TIACARCNSWCWASPVALNVQYAPRDVVRVKIKPLSEIHSNGNSVSLQCDFSSSHPKVEVQ
FFWEKNGRLLGKESQLNFDSISPEDAGSYSCWVNNSIGQTASKAWTLEVLVYAPRRLRVSM
SPGDQVMGKSAATLTCESDANPPVSHYIWFWDWNNQSLPHHSQKLRLEPVKVQHSGAYWCQ
GTNSVKGKRSPLSTLTVYYSPEITIGRRVAVGLGSCLAAILILAI CGLKLRWRKRTQSQQG
LQENSSGQSFFVRNKKVRRAPLSEGPSLGCYNPMMEDGISYTTLRFPEMNI PRTGDAES
SEMQRPPRTCDDTVTYSALHKRQVGDYENVI PDFPEDEGIHYSELIQFGVGERPQAQENV
DYVILKH

Signal sequence.

Amino acids 1-19.

Transmembrane domain.

Amino acids 685-705.

Immunoglobulin domain.

Amino acids 154-221, 258-311, 346-398, 435-486, 522-573, 609-611.

N-glycosylation site.

Amino acids 67-70, 101-104, 112-115, 135-138, 164-167, 231-234, 363-366, 445-448, 479-482, 574-577, 634-637, 724-727.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 420-423.

Protein kinase C phosphorylation site.

Amino acids 21-23, 45-47, 68-70, 79-81, 125-127, 137-139, 194-196, 241-243, 285-287, 304-306, 641-643, 764-766.

FIGURE 51B**Casein kinase II phosphorylation site.**

Amino acids 69-72, 79-82, 123-126, 200-203, 249-252, 270-273, 347-350, 452-455, 562-565, 601-604, 628-631, 789-792.

Tyrosine kinase phosphorylation site.

Amino acids 788-796.

N-myristoylation site.

Amino acids 392-397, 522-527, 567-572, 578-583, 655-660, 691-696, 693-698, 720-725, 759-764, 819-824.

Amidation site.

Amino acids 684-687.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 386-396.

FIGURE 53

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA227752
><subunit 1 of 1, 368 aa, 1 stop
><MW: 40660, pI: 8.10, NX(S/T): 3
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MVLEVSDHQVLNDAEVAALLENFSSSYDYGENESDSCCTSPPCPQDFSLNFDRAFLPALY
SLLFLLGLLGN GAVAAVLLSRRTALSSTDTFLLHLAVADTLLVLTLPLWAVDAAVQWVFG
SGLCKVAGALFNINFYAGALLLACISFDRYLNIVHATQLYRRGPPARVTLTCLAVWGLCL
LFALPDFIFLSAHHDERLNATHCQYNFPQVGRTRALRVLQLVAGFLLPLLMAYCYAHILA
VLLVSRGQRRRLAMRLVVVVVAFALCWTPTYHLVVLVDILMDLGALARNCGRESRVDAK
SVTSGLYMHCCLNPLLYAFVGVKFRERMWMLLLRLGCPNQRGLQRQPSSRRDSSWSET
SEASYSGL
```

Transmembrane domain.

Amino acids 54-74, 90-110, 129-149, 168-188, 216-236, 260-280, 303-323.

Seven transmembrane receptor domain.

Amino acids 70-318.

N-glycosylation site.

Amino acids 22-25, 32-35, 199-202.

Glycosaminoglycan attachment site.

Amino acids 304-307,

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 352-355.

Protein kinase C phosphorylation site.

Amino acids 80-82, 350-352, 351-353.

Casein kinase II phosphorylation site.

Amino acids 25-28, 86-89, 294-297, 351-354, 356-359.

N-myristoylation site.

Amino acids 67-72, 72-77, 120-125, 128-133.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 134-144.

FIGURE 54

DNA119476

GAGGGAAGAACACAATGGATCTGGTGCTAAAAAGATGCCTTCTTCATTTGGCTGTGATAG
GTGCTTTGCTGGCTGTGGGGGCTACAAAAGTACCCAGAAAACAGGACTGGCTTGGTGCT
CAAGGCAACTCAGAACCAAAGCCTGGAACAGGCAGCTGTATCCAGAGTGGACAGAAGCCC
AGAGACTTGACTGCTGGAGAGGTGGTCAAGTGTCCCTCAAGGTCAATGATGGGCCTA
CACTGATTGGTGCAAATGCCTCCCTTCTCTATTGCCTTGAACCTCCCTGGAAGCCAAAAGG
TATTGCCAGATGGGCAGGTTATCTGGGTCAACAATACCATCATCAATGGGAGCCAGGTGT
GGGGAGGACAGCCAGTGTATCCCAGGAAACTGACGATGCCTGCATCTTCCCTGATGGTG
GACCTTGCCCATCTGGCTCTTGGTCTCAGAAGAGAAGCTTTGTTTATGTCTGGAAGACCT
GGGGCAATACTGGCAAGTTCTAGGGGGCCAGTGTCTGGGCTGAGCATTTGGGACAGGCA
GGGCAATGCTGGGCACACACACCATGGAAGTACTGTCTACCATCGCCGGGGATCCCGGA
GCTATGTGCTCTTGTCTCATTCCAGCTCAGCCTTACCATTACTGACCAGGTGCCTTTCT
CCGTGAGCGTGTCCAGTTGCGGGCCTTGGATGGAGGGAAACAAGCACTTCTGAGAAATC
AGCCTCTGACCTTTGCCCTCCAGCTCCATGACCCAGTGGCTATCTGGCTGAAGCTGACC
TCTCTACACCTGGGACTTTGGAGACAGTAGTGAACCTGATCTCTCGGGCACTTGTGG
TCACTCATACTTACCTGGAGCCTGGCCAGTCACTGCCAGGTGGTCTGCAGGCTGCCA
TTCTCTCACTCCCTGTGGCTCCTCCCGAGTCCAGGCACCACAGATGGGCAAGGCCAA
CTGCAGAGGCCCTAACACCACAGCTGGCCAAGTGCCTACTACAGAAGTTGTGGGTACTA
CACCTGGTCAGGCGCCAAGTGCAGAGCCCTCTGGAACCACATCTGTGCAGGTGCCAACA
CTGAAGTCATAAGCACTGCACCTGTGCAGATGCCAAGTGCAGAGACAGGTATGACAC
CTGAGAAGGTGCCAGTTTTCAGAGGTCAATGAGTACCACACTGGCAGAGATGTCAACTCCAG
AGGCTACAGGTATGACACCTGCAGAGGTATCAATTGTGGTGCTTTCTGGAACCACAGCTG
CACAGGTAACAATACAGAGTGGGTGGAGACCACAGCTAGAGAGCTACCTATCCCTGAGC
CTGAAGGTCCAGATGCCAGCTCAATCATGTCTACGGAAAGTATTACAGGTTCCTGGGCC
CCCTGCTGGATGGTACAGCCACCTTAAGGCTGGTGAAGAGACAAGTCCCCCTGGATTGTG
TTCTGTATCGATATGGTTCCCTTTCCGTACCCCTGGACATGTCCAGGTATTGAAAGTG
CCGAGATCCTGCAGGCTGTGCCGTCCGGTGAGGGGGATGCATTTGAGCTGACTGTGTCT
GCCAAGCGGGCTGCCAAGGAAGCCTGCATGGAGATCTCATCGCCAGGGTGCCAGCCCC
CTGCCAGCGGCTGTGCCAGCCTGTGCTACCCAGCCAGCCTGCCAGCTGGTTCTGCACC
AGATACTGAAGGGTGGCTCGGGGACATACTGCCTCAATGTGTCTCTGGCTGATACCAACA
GCCTGGCAGTGGTCAGCACCCAGCTTATCATGCCTGGTCAAGAAGCAGGCCTTGGGCAGG
TTCCGCTGATCGTGGGCATCTTGTGGTGTGATGGCTGTGGTCTTGCATCTCTGATAT
ATAGGCGCAGACTTATGAAGCAAGACTTCTCCGTACCCAGTTGCCACATAGCAGCAGTC
ACTGGCTGCGTCTACCCGCATCTTCTGCTCTTGTCCATGGTGAGAACAGCCCCCTCC
TCAGTGGGCAGCAGGTCTGAGTACTCTCATATGATGCTGTGATTTTCTGGAGTTGACAG
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AGAGCCTGA

FIGURE 55A

><Thu Jul 20 10:27:08 2000 DNA119476 [min]
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119476
><subunit 1 of 1, 661 aa, 1 stop
><MW: 70255, pI: 5.52, NX(S/T): 5

MDLVLKRCLLHLAVIGALLAVGATKVPNRQDWLGVSRQLRTKAWNRQLYPEWTEAQRDC
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VYPQETDDACIFPDGGPCPSGWSQKRSFVYVWKTWGQYQVLGGPVSGLSIGTGRAMLG
THTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQPLTF
ALQLHDPSGYLAEDLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTS
CGSSPVPGT TDGHRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVIS
TAPVQMPTAESTGMTPPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAAQVTT
TEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCVLYRY
GSFSVTLDIVQGISAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQR
CQPVLFPSPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLQVPLIV
GILLVLMVAVLASLIYRRRLMKQDFSVLPQLPHSSSHWLRRLPRIFCSCPIGENSPLLGGQ
V

Signal Sequence.

Amino acids 1-20.

Transmembrane Domain.

Amino acids 594-614.

N-glycosylation site.

Amino acids 81-84, 106-109, 111-114, 321-324, 568-571.

Glycosaminoglycan attachment site.

Amino acids 504-507.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 191-194.

Protein kinase C phosphorylation site.

Amino acids 67-69, 93-95, 144-146, 174-176, 427-429, 463-465.

Casein kinase II phosphorylation site.

Amino acids 208-211, 279-282, 388-391, 401-404, 419-422, 427-430, 570-573.

FIGURE 55B

N-myristoylation site.

Amino acids 16-21, 63-68, 79-84, 164-169, 173-178, 267-272, 308-313, 325-330, 334-339, 338-343, 386-391, 399-404, 412-417, 492-497, 560-565, 588-593.

FIGURE 56A

DNA254890

CAGTCGGCACCGGCGAGGCCGTGCTGGAACCCGGGCTCAGCCGCAGCCGCAGCGGGGCC
GACATGACGACAGCTCCCAGGAGCCCCCGCCGGCCCCCTCCAGGCGGGCAGTGGAGET
GGCCCCGGCCCTGGGCGGCCATGCGCAGCACCACGCTCCTGGCCCTGCTGGCGCTGGTC
TTGCTTFACTTGGTGTCTGGTGCCCTGGTGTTCGGGGCCCTGGAGCAGCCCCACGAGCAG
CAGGCCAGAGGGAGCTGGGGGAGGTCCGAGAGAAGTTCCTGAGGGCCATCCGTGTGTG
AGCGACCAGGAGCTGGGCTCCTCATCAAGGAGGTGGCTGATGCCCTGGGAGGGGGTGGC
GACCCAGAAACCAACTCGACCAGCAACAGCAGCCACTCAGCCTGGGACCTGGGCGAGCGCC
TTCTTTTCTCAGGGACCATCATCACCACCATCGGCTATGGCAATGTGGCCCTGCGCACA
GATGCCGGGCGCCTCTTCTGCATCTTCTATGCGCTGGTGGGGATTCGCTGTTTGGGATC
CTACTGGCAGGGGTGCGGGACCGGCTGGGCTCCTCCTGCGCCATGGCATCGGTACATT
GAAGCCATCTTCTTGAAGTGGCAGCTGCCACCGGAGCTAGTAAGAGTGTGTGGCGATG
CTTTTCTGCTGATCGGCTGCCTGCTCTTTGTCTCAGCCCCAGTTTCGTGTTCTGCTAT
ATGGAGGACTGGAGCAAGCTGGAGGCCATCTACTTTGTATAGTGACGTTACCAACCGTG
GGCTTTGGCGACTATGTGGCCGGCGGACCCAGGAGGACTCCCGGCCATCAGCCG
CTGGTGTGGTTCTGGATCCTGCTCGGCTGGCTTACTTCGCCTCAGTGCTCACCACCATC
GGAACTGGCTGCGAGTAGTGTCCCGCCGCACTCGGGCAGAGATGGGCGGCCCTCAGGCT
CAGGCTGCCAGCTGGACTGGCACAGTGACAGCGCGGTGACCCAGCGAGCCGGGCCCCGCC
GCCCCGCGCCGGAGAAGGAGCAGCCACTGCTGCCTCCACCGCCCTGTCCAGCGCAGCCG
CTGGGCAGGCCCGATCCCCTTCGCCCCGAGAAGGCTCAGTGCCCTCCCCGCCACG
GCCTCGGCCCTGGATTATCCAGCGAGAACCTGGCCTTCATCGACGAGTCTCGGATACG
CAGAGCGAGCGCGGCTGCCCGTGCCTCGCGCCGAGAGGTGCGCCGCGCCAAATCCC
CCCAGGAAGCCCGTGGCGCCCCGCGGCCCGGGCTCCCCGAGCAAAGGCGTGCCTGGTG
TAGGGGCAGGATCCCTGGCCGGGCTCTCAAGGGCTTCGTTCTGCTCTCCCCGGCATGC
CTGGCTGTTTGACCAAAGAGCCCTCTTTCCACGAGACTGAAGTCTGGGGAGGAGGCTAC
AGTTGCCCTCTCCGCTCCTCCCTGGCCCCGGCCCTCCCTCACTTCCATCCATCTCTAGA
CCCCCCAAAGGCTTTCTGTGTGCTGCCCCGGGCGGGTGTATCCCTCAGCACCCTCAG
ACTGTGCCCTCAAAGCCTGCATCAATAAATGAAAACGGTCTGCACCCTGCGGGCGTGACG
CTCCCCGACGCGAGTGGGTGTGGAATTGCTTTCTCGGGCCACCGTGGGGGCACCTCTGG
CCTCCCGTGACCCCCAGGCCGAGGGTCCCCGGGCACCCAGGTCGGTCAAGTCTCGGCCCT
CTCAGGCCCGCTCTCTGCCTGGAGGAGACTGTGTAGGGTCCGGCGTGGGGATCAGCCGG
GATGGGCTGCGCGTCTCCAGCCTCTGCACACACATTTGGCGGGTGGGGTGCAGGGAGGGAG
AGGCAGGGGAGAGAGAATGGCATCTCGCGTGGAGGGCTGTGCTTTGAACTCTCCAGCGC
GAGAGACCCTGCCCGCCCCCTTCTGGAGCGTTGACTCCCTTCTCGTCTCGAGGCCCTGT
GGCGTCTGGGTCCGTGGGGCAGAACCATGGAGGAAAAGCCTTCGAAAGTGTGCTCAAG
TCTTCCGACCGCCAAAGGCTCGGACGAGGAGAGCGTGATAGCGACACTCGGGACCTGTGG
ACCACGACCACGCTGTCCCAGGCACAGCTGAACATGCCGCTGTCCGAGGTCTGCGAGGGC
TTCGACGAGGAGGGCCGCAACATTAGCAAGACCCGCGGGTGGCACAGCCCCGGGGCGGGG
TCGTTGGACGAGGGGTACAAGGCCAGCCACAAGCCGGAGGAAGTGGACGAGCACGCGCTG
GTGGAGCTGGAGTTGCACCGCGGCGAGCTCCATGGAATCAATCTGGGGGAGAAGGACACT
GCATCCAGATCGAGGCCGAAAAGTCTTCTCAATGTTCATCACTCAATATTGCGAAGCAC
ATGCCCATCGAGCTACTGGGCAGAGCAGCAGAGCAGGCTGCCACTGCCCTGATGGAA
CTCATGGAGAATGAAGCTCTGGAAATCCTCACCAAAGCCCTCCGGAGCTACCAGTTAGGG
ATCGGCAGGGACCACTTCTGACTAAGGAGCTGCAGCGATACATCGAAGGGCTCAAGAAG

FIGURE 56B

CGCCGGAGCAAGAGGCTGTACGTGAATTAAAAACGCCACCTTGGGCTCGAGCAGCGACCC
GAACCAGCCCCGTGCCAGCCCGGTCCCCAGACCCAAGCCTGACCCCATCCGAGTGAATT
TGAGTCCTAAAGAAATAAAGAGTCGATGCATGAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAA

FIGURE 57

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA254890
><subunit 1 of 1, 419 aa, 1 stop
><MW: 45189, pI: 9.15, NX(S/T): 2

MTTAPQEPPARPLQAGSGAGPAPGRAMRSTLLALLLVLLYLVS GALVFRAL EQPHEQQ
AQRELGEVREKFLRAHPCVSDQELGLLIKEVADALGGGADPETNSTSNSSHS AWDLGSAF
FFSGTIITTTIGYGNVALRTDAGRLFCIFYALVGIPLFGILLAGVGDRLGSSLRHGIGHIE
AIFLKWHVPELVRLSAMLFLIGCLLFVLTPTFVFCYMEDWSKLEAIYFVIVTLTTVG
FGDYVAGADPRQDSPAYQPLVWFWILLGLAYFASVLTIGNWLRVVSRRTRAEMGGLTAQ
AASWTGTVTARVTQRAGPAAPPPEKEQPLLPPPCPAQPLGRPRSPSPPEKAQLPSPPTA
SALDYPSENLAFIDESSDTQSERGCPLPRAPRRRRPNPPRKPVRPRGPRPRDXGVPV

Signal sequence.

Amino acids 1-46.

Transmembrane domain.

Amino acids 114-134, 145-165, 190-210, 224-244, 259-279.

N-glycosylation site.

Amino acids 104-107, 108-111.

Glycosaminoglycan attachment site.

Amino acids 17-20.

Protein kinase C phosphorylation site.

Amino acids 171-173, 287-289, 309-311, 313-315, 381-383.

Casein kinase II phosphorylation site.

Amino acids 80-83, 112-115, 224-227, 290-293, 347-351, 361-364,
379-382.

N-myristoylation site.

Amino acids 124-129, 158-163, 295-300, 306-311.

Amidation site.

Amino acids 392-395.

Prokaryotic membrane lipoprotein, lipid attachment site.

Amino acids 196-206.

FIGURE 58A

getseq sst.DNA219240
GCCAACACTGGCCAAACAGAAGCCTCCGGTCCGGCTGCAGTGCCCAAGTCCCATGGCGAG
GGCAGCCCCAGTGGCCGTCCGGCTGTAGGTCCGCATGCCGGGCACCGCACCAGGCGTCT
AGCAGATGGACACAGGAAGATCCAGAAGCTAGTGGCACATCTAGCAACAGAGCCAGATCA
GAACCCAGATGCTAAACTCCTGCTGGACTGCAGAGGAGAGGGATTTCAGTCTTCTCCTGAT
GTCGATTGCGATTCTGCTGGGAGCTCAAGACGGGCGAGCTGCCCGAGATCTCTTCGAGA
TACCCAGGGGAGGAGAGATGGGCAGGATTTAGTAGGACAACCTCGGTTACTAATGACTT
GGCGCTGGCTGCGACCCCCCGGAAATCAGGTGCAAGCATGTTGCTGTAGGTACCTG
AGTTGACACCGAAGGTGCCTAAAGATGCTGAGCGCGTGGTTTCTCAGTGTGTTAAC
GTGGCCGGGATCTTACAGACAGAGAGTGCAGAACTGCCAAAGACATTTGCAAGATCCGC
TGCTGTGCGAAGAAAAGGAAAACGTAATCAACTGTGAGAACAAGGATTTACA
ACAGTTAGCCTGCTCCAGCCCCCAGTATCGAATCTATCAGCTTTTCTCAATGGAAAC
CTCTTGACAAGACTGTATCAAACGAATTTGTCAATTACTCCAACGCGGTGACTCTTCAC
CTAGGTAAACAACGGGTTACAGGAGATCCGAACGGGGCATTTCAGTGGCCTGAAAACCTC
AAAAGACTGCATCTCAACAACAACAGCTTGAGATATTGAGGGAGGACACCTTCTTAGGC
CTGGAGAGCCTGGAGTATCTCCAGGCCGACTACAATTACATCAGTGCATCGAGGCTGGG
GCATTCAGCAAACCTAAACAAGCTCAAAGTGCTCATCTGAATGACAACTTCTGCTTTCA
CTGCCAGCAATGTGTTCCGCTTTGTCTGCTGACCCACTTAGACCTCAGGGGGAATAGG
CTAAAAGTAATGCCTTTTGTGCTGGCGTCTTGAACATATTGGAGGGATCATGGAGATTCAG
CTGGAGGAAAATCCATGGAATTGCACTTGTGACTTACTTCTCTCAAGGCCTGGCTAGAC
ACCATAACTGTTTTTGTGGGAGAGATTGTCTGTGAGACTCCCTTAGGTTGCATGGGAAA
GACGTGACCCAGCTGACCAGGCAAGACCTCTGTCCCAGAAAAGTGCCAGTGATTCCAGT
CAGAGGGGCGCCATGCTGACACCCACGTCAAAGGCTGTCACCTACAATGAATCCTGCT
CTCAACCCAACAGGGCTCCGAAAGCCAGCCGGCCGCCCCAAAATGAGAAATCGTCCAAC
CCCCGAGTACTGTGTCAAAGGACAGGCAAAGTTTTGGACCCATCATGGTGTACCAGACC
AAGTCTCCTGTGCCCTCTCACCTGTCCCAGCAGCTGTGTCTGCACCTCTCAGAGCTCAGAC
AATGGTCTGAATGTAAACTGCCAAGAAAGGAAGTCACTAATATCTCTGACCTGCAGCCC
AAACCGACAGTCCAAAGAAACTCTACCTAACAGGGAACATCTTCAAACCTGTCTATAAG
AATGACCTCTTAGAATACAGTTCTTTGGACTTACTGCACTTAGGAAAACAACAGGATTGCA
GTCAATTCAGGAAGGTGCCTTTACAAACCTGACCAGTTTACGCAGACTTTATCTGAATGGC
AATTACCTTGAAGTGTGTACCCTTCTATGTTGATGGACTGCAGAGCTTGCAATATCTC
TATTTAGAGTATAATGTCATTAAGGAAATTAAGCCTCTGACCTTTGATGCTTTGATTAAC
CTACAGCTACTGTTTCTGAAACAACAACCTTCTTCGGTCTTACCTGATAATATATTTGGG
GGGACGGCCCTAACAGGCTGAATCTGAGAAAACAACCAATTTTTCTCACCTGCCCGTGAAA
GGGTTCTGGATCAGCTCCCAGCTTTTATCCAGATAGATCTGCAGGAGAACCCCTGGGAC
TGTACCTGTGACATCATGGGGCTGAAAGACTGGACAGAACATGCCAATCCCCTGTCTATC
ATTAATGAGGTGACTTGCGAATCTCCTGCTAAGCATGCAGGGGAGATACTAAAATTTCTG
GGGAGGGAGGCTATCTGTCCAGACAGCCCAAACCTGTGAGATGGAACCGTCTTGTCAATG
AATCACAATACAGACACACCTCGGTGCTTAGTGTCTCCTAGTTCCTATCTGAACTA
CACACTGAAGTTCACCTGTCTGCTTAATCTGGGATGCTGTTGTTTTTCTATCTTATCT
GTCTGTTTTGGGGCTGGTTTATTCGTCTTTGCTTGAACCGCCGAAAGGGAGTGCCGAGC
GTTCCAGGAATACCAACAACCTTAGACGTAAGCTCCTTCAATTACAGTATGGGTCTTAC
AACACTGAGACTCACGATAAAAACAGACGGCCATGTCTACAACATATCCCCCACCTGTG
GGTCAGATGTGCCAAAACCCATCTACATGCAGAAGGAAGGAGACCCAGTAGCCTATTAC
CGAAACCTGCAGGAGTCAAGACCAGCCTAGAGAACATATGGAGACCCTGTCTTCACAAA

FIGURE 58B

AAATAAAAAAGTCAGCCAAGCGTGGTGGTGTGTGCCTGTAGTTACTTAGGAGGCTGAGGC
AGGACGATCGCTTAAGCCAGGAGTTTGAGGCTGTGGTGAGCTACAATTGCGCCACTGCA
CGCCAGCCTGGCTACAGAACGAGACCCTGCCTCTCTAAAAAAAAAAAAAAAAAAAAA

FIGURE 59A

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA219240

><subunit 1 of 1, 733 aa, 1 stop

><MW: 82695, pI: 8.37, NX(S/T): 6

MLSGVWFLSVLTVAGILQTESRKTAKDICKIRCLCEEKENVLNINCENKGFTTVSLLOPP
QYRIYQLFLNGNLLTRLYPNEFVNYSNAVTLHLGNNGLQEIRTGAFSGLKTLKRLHLNNN
KLEILREDTFLGLESLEYLQADYNYISAI EAGAFSKLNKLVLI LNDNLLLSLPSNVFRF
VLLTHLDLRGNRLKVMFPAGVLEHIGGIMEIQLEENPWNTCDLLPLKAWLDTITVFVGE
IVCETPFRLHGKDVTLQTRQDLCPRKASADSSQRGSHADTHVQRLSPTMNPALNPTRAPK
ASRPPKMRNRPTPRVTVSKDRQSFPGPIMVYQTKSPVPLTCPSSCVCTSQSSDNGLNVNCQ
ERKFTNISDLQPKPTSPKKLYLTGNYLQTVYKNDLLEYSSDLLHLGNNRIAVIQEGAF
NLTSLRRLYLNGNYLEVLPSPMFDGLQSLQYLYLEYNVIKEIKPLTFDALINLQLLFLNN
NLLRSLPDNIFGGTALTRLNLRNNHFSHLPVKGVLQDLPAFIQIDLQENPWDCTCDIMGL
KDWTEHANSPI INEVTCESPAKHAGEILKFLGREAI CPDSPNLS DGTVLSMNHNTDTPR
SLSVSPSSYPELHTEVPLSVLILGLLVVFILSVCFGAGLFVFLKRRKGVPSVPRNTNNL
DVSSFQLQYGSYNTETHDKTDGHVYNYIPPPVGMQCNPIYMQKEGDPVAYYRNLQEFKT
SLENIWRPCLHKK

Signal sequence.

Amino acids 1-18.

Transmembrane domain.

Amino acids 161-181, 466-486, 616-636.

N-glycosylation site.

Amino acids 84-87, 219-222, 366-369, 421-424, 583-586.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 362-365.

Protein kinase C phosphorylation site.

Amino acids 21-23, 24-26, 111-113, 272-274, 312-314, 376-378,
424-426, 598-600.

Casein kinase II phosphorylation site.

Amino acids 24-27, 147-150, 184-187, 258-261, 267-270, 276-279,
399-402, 441-444, 485-488, 608-611, 720-723.

Tyrosine kinase phosphorylation site.

Amino acids 704-711.

FIGURE 59B

N-myristoylation site.

**Amino acids 15-20, 71-76, 104-109, 354-359, 417-422, 493-498,
587-592, 670-675.**

FIGURE 60A

getseq sst.DNA37151

AAGGAGGCTGGGAGGAAAGAGGTAAGAAAGGTTAGAGAACCTACCTCACATCTCTCTGGG
CTCAGAAGGACTCTGAAGATAACAATAATTTAGCCCATCCACTCTCCTTCCCTCCCAA
CACACATGTGCATGTACACACACACATACACACATACACCTTCCCTCTCCTTCACTGAA
GACTCACAGTCACTCACTCTGTGAGCAGGTCATAGAAAAGGACACTAAAGCCTTAAGGAC
AGGCCTGGCCATTACCTCTGCAGCTCCTTTGGCTTGTGAGTCAAAAACATGGGAGGGG
CCAGGCACGGTGACTCACACCTGTAATCCCAGCATTTTGGGAGACCGAGGTGAGCAGATC
ACTTGAGGTGAGGAGTTCGAGACCAGCCTGGCCAACATGGAGAAACCCCCATCTCTACTA
AAAATACAAATTTAGCCAGGAGTGGTGGCAGGTGCCTGTAATCCCAGCTACTCAGGTGG
CTGAGCCAGGAGAATCGCTTGAATCCAGGAGGCGGAGGATGCAGTCAGCTGAGTGCACCG
CTGCACTCCAGCCTGGGTGACAGAAATGAGACTCTGTCTCAAACAAACAAACCGGGAGGA
GGGGTAGATACTGCTTCTCTGCAACCTCCTTAACCTGTCATCCTTCTTCCAGGGCTGC
CCCTGATGGGGCTGGCAATGACTGAGCAGGCCAGCCCCAGAGGACAAGGAAGAGAAGG
CATATTGAGGAGGGCAAGAAGTGCAGCCCGGTGTAGAATGACTGCCTGGGAGGGTGGTT
CCTTGGGCCCTGGCAGGGTTGCTGACCCTTACCCTGCAAAACAAAGAGCAGGACTCCA
GACTCTCCTTGTGAATGGTCCCCTGCCCTGCAGCTCCACCATEAGGCTTCTCGTGGCCCC
ACTCTTGCTAGCTTGGGTGGCTGGTGGCACTGCCACTGTGCCCCGTGGTACCCTGGCATGT
TCCCTGCCCCCCCTCAGTGTGCCTGCCAGATCCGGCCCCGTGGTATACGCCCCGCTCGTCTA
CCGCGAGGCTACCCTGTGGACTGCAATGACCTATTCTGACGGCAGTCCCCCGGCACT
CCCCGCAGGCACACAGACCCTGCTCCTGCAGAGCAACAGCATTGTCCGTGTGGACCAGAG
TGAGCTGGGCTACCTGGCCAATCTCACAGAGCTGGACCTGTCCAGAACAGCTTTTCGGA
TGCCCGAGACTGTGATTTCCATGCCCTGCCCCAGCTGCTGAGCCTGCACCTAGAGGAGAA
CCAGCTGACCCGGCTGGAGGACCACAGCTTTGCAGGGCTGGCCAGCCTACAGGAACCTTA
TCTCAACCACAACCAGCTCTACCGCATGCCCCAGGGCCTTTTCTGGCCTCAGCAACTT
GCTGCGGCTGCACCTCAACTCCAACCTCTGAGGGCCATTGACAGCCGCTGGTTTGAAT
GCTGCCCAACTTGGAGATACTCATGATTGGCGGCAACAAGGTAGATGCCATCCTGGACAT
GAACTTCCGGCCCCCTGGCCAACCTGCGTAGCCTGGTGTAGCAGGCATGAACCTGCGGGA
GATCTCCGACTATGCCCTGGAGGGGCTGCAAAGCCTGGAGAGCCTCTCCTTCTATGACAA
CCAGCTGGCCCCGGGTGCCAGGCGGGCACTGGAACAGGTGCCCGGGCTCAAGTTCTTAGA
CCTCAACAAGAACCCTCCAGCGGGTAGGGCCGGGGGACTTTGCCAACATGCTGCACCT
TAAGGAGCTGGGACTGAACAAATGGAGGAGCTGGTCTCCATCGACAAGTTTGCCTGGT
GAACCTCCCGAGCTGACCAAGCTGGACATACCAATAACCCACGGCTGTCTTTCATCCA
CCCCCGGCCTTCCACCACCTGCCCCAGATGGAGACCCTCATGCTCAACAACAACGCTCT
CAGTGCCTTGCACCAGCAGACGGTGGAGTCCCTGCCCAACCTGCAGGAGGTAGGTCTCCA
CGGCAACCCCATCCGCTGTGACTGTGTATCCGCTGGGCCAATGCCACGGGCACCCGTGT
CCGCTTCATCGAGCCGCAATCCACCCTGTGTGCGGAGCCTCCGGACCTCCAGCGCTCCC
GGTCCGTGAGGTGCCCTTCCGGGAGATGACGGACCCTGTTTGGCCCTCATCTCCCACG
AAGCTTCCCCCAAGCCTCCAGGTAGCCAGTGGAGAGAGCATGGTGTGCTGATTGCGGGC
ACTGGCCGAACCCGAACCCGAGATCTACTGGGTCACTCCAGCTGGGCTTCGACTGACACC
TGCCCATGCAGGCAGGAGGTACCGGGTGTACCCCGAGGGGACCTGGAGCTGCGGAGGGT
GACAGCAGAAGAGGCAGGGCTATACACCTGTGTGGCCAGAACCTGGTGGGGGCTGACAC
TAAGACGGTTAGTGTGGTTGTGGGCCCTGCTCTCCTCCAGCCAGGCAGGGACGAAGGACA
GGGGCTGGAGCTCCGGGTGCAGGAGACCCACCCCTATCACATCCTGCTATCTTGGGTAC
CCCACCAACACAGTGTCCACCAACCTCACCTGGTCCAGTGCCTCCTCCCTCCGGGGCCA

FIGURE 60B

GGGGCCACAGCTCTGGCCCGCCTGCCTCGGGGAACCCACAGCTACAACATTACCCGCCT
CCTTCAGGCCACGGAGTACTGGGCCTGCCTGCAAGTGGCCTTTGCTGATGCCACACCCA
GTGGCTTGTGTATGGGCCAGGACCAAAGAGGCCACTTCTTGCCACAGAGCCTTAGGGGA
TCGTCCCTGGGCTCATTGCCATCCTGGCTCTCGCTGTCTTCTCCTGGCAGCTGGGCTAGC
GGCCACCTTGGCACAGGCCAACCCAGGAAGGGTGTGGGTGGGAGGCGGCCTCTCCCTCC
AGCCTGGGCTTCTGGGGCTGGAGTGCCCTTCTGTCCGGGTGTGTCTGCTCCCCTCGT
CCTGCCCTGGAATCCAGGGAGGAAGCTGCCCAGATCCTCAGAAGGGGAGACACTGTTGCC
ACCATTTGCTCAAAATTTCTGAAGCTCAGCCTGTTCTCAGCAGTAGAGAAATCACTAGGA
CTACTTTTTACCAAAGAGAAGCAGTCTGGGCCAGATGCCCTGCCAGGAAAGGGACATGG
ACCCACGTGCTTGAGGCCTGGCAGCTGGGCCAAGACAGATGGGGCTTTGTGGCCCTGGGG
GTGCTTCTGCAGCCTTGAAAAAGTTGCCCTTACCTCCTAGGGTCACCTCTGCTGCCATTC
TGAGGAACATCTCCAAGGAACAGGAGGGACTTTGGCTAGAGCCTCCTGCCTCCCCATCTT
CTCTCTGCCAGAGGCTCCTGGGCCTGGCTTGGCTGTCCCTACCTGTGTCCCCGGGCTG
CACCCCTCCTCTTCTTTCTCTGTACAGTCTCAGTTGCTTGCTCTTGTGCCTCCTGGG
CAAGGGCTGAAGGAGGCCACTCCATCTCACCTCGGGGGCTGCCCTCAATGTGGGAGTGA
CCCCAGCCAGATCTGAAGGACATTTGGGAGAGGGATGCCCAGGAACGCCCTCATCTCAGCA
GCCTGGGCTCGGCATTCCGAAGCTGACTTCTATAGGCAATTTTGTACCTTTGTGGAGAA
ATGTGTACCTCCCCAACCCGATTCACTCTTTCTCCTGTTTTGTAAAAAATAAAAAATA
AATAATAACAATAAAAAA

FIGURE 61A

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA37151
><subunit 1 of 1, 713 aa, 1 stop
><MW: 78889, pI: 7.49, NX(S/T): 4
MRLLVAPLLLAWVAGATATVPVFWHVPCPPQCACQIRPWYTPRSSYREATVDCNDLFL
TAVPPALPAGTQTLQLLSNSIVRVDQSELGYLANLTELDSLQNSFSDARDCDFHALPQLL
SLHLEENQLTRLEDHSFAGLASLQELYLNHNQLYRIAPRAFSGLSNLLRLHLNSNLLRAI
DSRWFEMLPNLEILMIGGNKVDAILDMMNFRPLANLRSVLVLAGMNLREISDYALEGLQSL
SLSFYDNQLARVPRRALEQVPGKFLDLNKNPLQRVGPGDFANMLHLKELGLNNMEELVS
IDKPALVNLPELTKLDITNNPRLSFIHPRAFHLPQMETMLMNNALSALHQQTVESLPN
LQEVGLHGNPIRCDCVIRWANATGTRVRFIEPQSTLCABPPDLQRLFPVREVPFREMTHC
LPLISPRSFPPSLQVSGESMVLHCRALAEPEPEIYWVTPAGLRLTPAHAGRRYRVYPEG
TLELRRVTAEEAGLYTCVAQNLVGADTKTVSVVVGRRALLQPRDEGQGLELRVQETHPYH
ILLVSWVTPPNTVSTNLTWSSASSLRGQATALARLPRGTHSYNITRLLQATEYWACLQVA
FADAHTQLACVWARTKEATSHRALGDRPGLIAILALAVLLLAAGLAAHLGTGQPRKGVG
GRRPLPRAWAFWGSAPSVRVVSAPLVLPWNPGRKLPKRSSEGETLLPPLSQNS
```

Signal sequence.

Amino acids 1-18.

Transmembrane domain.

Amino acids 628-648, 667-687.

Leucine rich repeat domain.

Amino acids 94-117, 118-141, 142-165, 166-189, 190-213, 214-237, 238-261, 262-285, 286-310, 311-335, 336-359, 360-407.

Immunoglobulin domain.

Amino acids 438-499.

N-glycosylation site.

Amino acids 94-97, 381-834, 555-558, 583-586.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 485-488.

Protein kinase C phosphorylation site.

Amino acids 42-44, 46-48, 425-427, 563-565, 678-680.

Casein kinase II phosphorylation site.

Amino acids 46-49, 51-54, 96-99, 104-107, 130-133, 142-145, 243-246, 313-316, 488-491, 700-703.

FIGURE 61B

Tyrosine kinase phosphorylation site.
Amino acids 532-539.

N-myristoylation site.
Amino acids 15-20, 493-498, 566-571.

Amidation site.
Amino acids 470-473, 660-663, 692-695.

FIGURE 62

getseq sst.DNA210233

GGCACGAGCCGGCAAGCCGAGCTAGGGTGAAAACCTGGGGGCGCACCAGG ATGTXXGACAG
AAAAGCAGAAGATGAGACTCTGTTCATTCACCTTTTCCTAGGCCCATCCTGTGGTCATCTT
TCCCCCTCCCATCATACTCCTCCTTCTGGAGCCTCTGCCGGCTTGGCTGTAATGGTGG
CACTTACCTGGATATTTAGTGGGAGGATGAAAGGCGAGACTCACCTACGCGGTGGGAC
AGATGGGGAGAGGAAAAGGCAGAGATGGCCAGGAGAGGGGTGCAGGACAAACCAGAGAG
GTTGGGTCAGGGGAAAAGGGTGGGGAGAAAGAGGGGTGCAGGCCCTGCAGGCCGGTTAGC
CAGCAGCTGCGGCCCTCCCGGGCCCTTGGCATCCAACCTTCGCAGACAGGGTACCAGCCTC
CTGGTGTGTATCATAGGATTTGTTACATAGTGTATGCATGATCTTCGTAAGGTTAAGA
AGCCGTGGTGGTGCACCATGACATCCAACCCGTATATATAAAGATAAATATATATATATA
TGATGTAAATTATGGCACGAGAAATTATAGCACTGAGGGCCCTGCTGCCCTGCTGGACC
AAGCAAAACTAAGCCTTTGGTTTGGGTATTATGTTTCGTTTGTATTATTGTTTGTTTTT
GTGGCTGTCTTATGTCGTGATAGCACAAGTGCCAGTCGGATTGCTCTGTATTACAGAAT
AGTGTTTTTAATTCATCAATGTTCTAGTTAATGTCTACCTCAGCACCTCCTCTTAGCCTA
ATTTTAGGAGGTTGCCCAATTTGTTTCTTCAATTTACTGGTTACTTTTTGTACAAAT
CAATCTCTTTCTCTCTTTCTCTCCTCCCCACCTCTCACCTTGCCCTCTCCATCTCCCTC
TCCCGCCCTCCCCTCCTCCTCTGGCTCCCCGTCTCATTTCTGTCCACTCCATTCTCTCT
CCCTCTCTCCTGCCCTCCTGCTGCCCCCTCCCCAGCCACTTCCCCGAGTTGTGCTTGCCG
CTCCTTATCTGTCTAGTTCGAAGCAGTTTCACTCGAAGTTGTGCAGTCTTGTTGCAG
CTTTCGCATCTGCCCTCGTTTCGTGTAGATTGACGCTTCTTTGTAAATTCAGTGTTT
CTGACAAGATTTAAAAAAAAAAAAAAAAAGGAAAAAAAAAAAAAAAA AAA

FIGURE 63

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA210233
><subunit 1 of 1, 145 aa, 0 stop
><MW: 15963, pI: 10.59, NX(S/T): 1
MSTSAPPLSLILGGCPILFLQFYWLLFCTNQSLSLFLSSPPLTLALSISLSRPPLLPLAP
RLISVHSILSPSLLPPAAPSPAHFPELCLPLLICSSSEAVSLÉVVQSWLQLSASAFVSCR
LTRFFVISVFLTRFKKKKRRKKKKKK
```

Signal sequence.

Amino acids 1-45.

Transmembrane domain.

Amino acids 54-74, 108-128.

N-glycosylation site.

Amino acids 30-33.

Protein kinase C phosphorylation site.

Amino acids 118-120.

Casein kinase II phosphorylation site.

Amino acids 95-98.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 5-15, 109-119.

FIGURE 64

getseq sst.DNA35918

CCCACGCGTCCGCACCTCGGCCCGGGCTCCGAAGCGGCTCGGGGGGCCCTTTCGGTCA
ACATCGTAGTCCACCCCTCCCATCCCCAGCCCCGGGATTTCAGGCTCGCCAGCGCCC
AGCCAGGGAGCCGGCCGGGAAGCGCGATGGGGGGCCCCAGCCGCTCGCTCCTGCTCCTGC
TCCTGCTGTTTCGCTGCTGCTGGGCGCCCGGGGGCCAACTCTCCAGGACGACAGCC
AGCCCTGGACATCTGATGAAACAGTGGTGGCTGGTGGCACCGTGGTGTCAAGTGCCAAG
TGAAAGATCAGGAGACTCATCCCTGCAATGGTCTAACCTGCTCAGCAGACTCTCTACT
TTGGGGAGAAGAGAGCCCTTCGAGATAATCGAATTCAGCTGGTTACCTCTACGCCCCAG
AGCTCAGCATCAGCATCAGCAATGTGGCCCTGGCAGACGAGGGCAGTACACCTGTCTAA
TCTTCACTATGCCTGTGCGAACTGCCAAGTCCCTCGTCACTGTGCTAGGAATTCACAGA
AGCCCATCATCACTGGTTATAAATCTTCATTACGGGAAAAAGACACAGCCACCCTAAACT
GTCAGTCTTCTGGGAGCAAGCCTGCAGCCCGGCTCACCTGGAGAAAGGGTGACCAAGAAC
TCCACGGAGAACCACCCGCATACAGGAAGATCCCAATGGTAAAACCTTCACTGTAGCA
GCTCGGTGACATTCCAGGTTACCCGGGAGGATGATGGGGCGAGCATCGTGTGCTCTGTGA
ACCATGAATCTCTAAAGGGAGCTGACAGATCCACCTCTCAACGCATTGAAGTTTTATACA
CACCAACTGCGATGATTAGGCCAGACCCTCCCCATCCTCGTGAGGGCCAGAAGCTGTGTC
TACACTGTGAGGGTCCGCGCAATCCAGTCCCCCAGCAGTACCTATGGGAGAAGGAGGGCA
GTGTGCCACCCCTGAAGATGACCCAGGAGAGTGCCCTGATCTTCCCTTTCCTCAACAAGA
GTGACAGTGGCACCTACGGCTGCACAGCCACCAGCAACATGGGCAGCTACAAGGCCTACT
ACACCCCTCAATGTTAATGACCCAGTCCGGTGCCTCCTCCTCCAGCACCTACCACGCCA
TCATCGGTGGGATCGTGGCTTTCAATGTCTTCTGCTGCTCATCATGCTCATCTTCTTG
GCCACTACTTGATCCGGCACAAAGGAACCTACCTGACACATGAGGCAAAGGCTCCGACG
ATGCTCCAGACGCGACACGGCCATCATCAATGCAGAAGGCGGGCAGTCAGGAGGGGACG
ACAAGAAGGAATATTTTCATCTAGAGGCGCCTGCCACTTCTGCGCCCCCAGGGGCCCT
GTGGGACTGCTGGGGCCGTACCAACCCGGACTTGTACAGAGCAACCGCAGGGCCGCC
CTCCGCTTGCTCCCCAGCCACCCACCCCTGTACAGAATGTCTGCTTTGGGTGCGGT
TTTGTACTCGGTTTGAATGGGGAGGGAGGGCGGGGGAGGGAGGGTTGCCCTCAG
CCCTTCCGTGGCTTCTCTGCATTTGGGTTATTATTATTTTGTAACAATCCCAAATCAA
ATCTGTCTCAGGCTGGAGAGGCAGGAGCCCTGGGGTGAGAAAAGCAAAAAACAACAAA
AAACA

FIGURE 65

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><Tue Nov 11 14:57:29 PST 1997 DNA35918 [min]
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA35918
><subunit 1 of 1, 398 aa, 1 stop
><MW: 43300, pI: 6.00, NX(S/T): 2
MGAPAASLLLLLLLLFACWAPGGANLSQDDSQPWTSDFTVVAGGTVVVKCQVKDHEDSSL
QWSNPAQQTLYFG EKRALRDNRIQLVTSTPHELSSISISNVALADEGEYTCISIFTMPVRTA
KSLVTVLGIPQKPIITGYKSSLREKDTATLNCQSSGSKPAARLTWRKGDQELHGEPTRIQ
EDPNGKIFTVSSSVTFQVTREDDGASIVCSVNHESLKGADRSTSQRIEVLVYPTAMIRPD
PPHPREGQKLLHCEGRGNPVPQQYLWEKEGSPPLKMTQESALIFPFLNKSDSGTYGCT
ATSNMGSYKAYYTLNVNDPSPVPSSTYHAIIGGIVAFIVFLLIMLIFLGHYLIRHKG
TYLTHEAKGSDDAPDADTAIINAEGGQSGGDDKKEYFI
```

Signal Sequence

Amino acids 1-20.

Transmembrane domain.

Amino acids 332-352.

Immunoglobulin domain.

Amino acids 43-112, 145-211, 247-301.

N-glycosylation site.

Amino acids 25-28, 290-293, 119-121, 141-143, 164-166, 215-217, 224-226, 307-309.

Casein kinase II phosphorylation site.

Amino acids 27-30, 35-38, 89-92, 141-144, 199-202, 388-391.

N-myristoylation site.

Amino acids 2-7, 23-28, 156-161, 218-223, 295-300, 298-303, 306-311, 334-339, 360-365, 385-390, 386-391.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 7-17.

FIGURE 66

getseq sst.DNA260038

CTTGGATCTGCCTGCCAGGCCATCCTGGGCGCTGCAGGAAGCAACATGACTTAGGTA
GCCCAGAGGTGCACCAGACATGATGCAGCAGCCGCGAGTGGAGACAGATAACCATCGGGC
TGGCGAGGGGCCACAGCAGGCAGTGCCTGGTCAGCCTGGGTCACGAGGCATGGCTGGGTG
CGCTGGTGGGTGAGCCACATGCCCCGAGCTGGATCCAGTGGTGGAGCACCTCGAACTGG
CGGCAACGGCTGCAGCGCCTGCTGTGGGGTCTGGAGGGGATACTCTACCTGCTGCTGGCA
CTGATGTGTGCCATGCACTCTTCACCACTGGCTCCACCTGCTGAGCTCCTTGTGGCCT
GTCGTGGCCGCGGTGTGGCGCCACCTGCTACCGGCTCTCCTGCTGCTGGTGCTCAGTGCT
CTGCCCTGCCCTCCTCTTCACGGCCTCCTTCCTGCTGCTCTTCTCCCACTGCTGAGCCTT
GTGGCCTCCTCACCTCCATGACTCACCCAGGCGACACTCAGGATTTGGATCAA TAGAAG
GGCAACCCCATCCCACTGCCTGTGTTTGTGAGCCCTGGCCTAGGGCCTGAGACCCACG
GGGAGAGGGAGGGCAATGGGATCAGGGCTCCCTGCCCTTGGCAGGGCCAGACCCCTAGTC
CCTAACAGGTAGGCTGGCCTG

FIGURE 67

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA260038
><subunit 1 of 1, 112 aa, 1 stop
><MW: 12573, pI: 6.85, NX(S/T): 0
MPPSWIQWSTSNWRQPLQRLWGLEGILYLLLALMLCHALFTTGSHLLSSLWPFVVAAVW
RHLLPALLLLVLSALPALLFTASFLLLFSTLLSLVGLLTSMTHPGDTQDLQ
```

Signal sequence.

Amino acids 1-40.

Transmembrane domain.

Amino acids 54-74, 70-90.

N-myristoylation site.

Amino acids 96-101.

Eukaryotic thiol (cysteine) proteases histidine active site.

Amino acids 37-47.

FIGURE 68

getseq sst.DNA334818

ACATGCGCCCTGACAGCCCAACAATGGCGGGCGCCCGCGGAGTCGCTGAGGAGGCGGAAGA
CTGGGTACTCGGATCCGGAGCCTGAGTCGCGCGCCCGCGCCGGGCGTGGCCCCGAGGCT
CTCCGGCCCATCTTCACACGGGCACCTTCTGGCTGACCCGGATCGTGCTCCTGAAGGCC
TAGCCTTCGTGTACTTCGTGGCATTCTGGTGGCTTCCATCAGAACAAGCAGCTCATCG
GTGACAGGGGGCTGCTTCCCTGCAGAGTGTTCCGAAGGACTTCAGCAGTACTTCCAGG
ACAGGACAAGCTGGGAAGTCTTCAGCTACATGCCACCATCCTCTGGCTGATGGACTGGT
CAGACATGAACCTCAACCTGGACTTGCTGGCTCTTCTCGGACTGGGCATCTCGTCTTTCG
TACTGATCACGGGTTGCGCCAACATGCTTCTCATGGCTGCCCTGTGGGGCCTTACATGT
CCCTGGTTAATGTGGCCATGTCTGGTACTCTTTCGGATGGGAGTCCAGCTTCTGGAGA
CGGGATTCTGGGGATCTTCTGTGCCCTCTGTGGACGCTGTCAAGGCTGCCCCAGCATA
CCCCACATCCCGGATGTCTGTGGGGCTTCCGGTGGCTGATCTTCAGGATCATGCTTG
GAGCAGGCTGATCAAGATCCGGGGGACCGGTGCTGGCAGACCTCACCTGCATGGACT
TCCACTATGAGACCCAGCCGATGCCCAATCCTGTGGCATACTACCTGCACCCTCACCT
GGTGGTTCATCGCTTCGAGACGCTCAGCAACCCTTCATCGAGCTCCTGGTGGCCTTCT
TCCTCTTCTCGGCCGGCGGGCGTGCATCATCCACGGGGTGCCTGCAGATCCTGTTCCAGG
CCGTCTCATCGTCAGCGGAACCTCAGCTTCTGAACTGGCTGACTATGGTGGCCAGCC
TGGCCTGCTTTGATGACGCCACCTGGGATTCTTGTTCCTCTGGGCCAGGCAGCCTGA
AGGACCGAGTTCGAGATGCAGAGGGACATCCGAGGGGCCCGCCGAGCCAGATTTCG
GCTCCGTGGTGGCGGTGCAGCCAACGTCTCGCTGGGCGTCTGCTGGCCTGGCTCAGCG
TGCCCGTGGTCTCAACTTGCTGAGCTCCAGGCAGGTATGAACACCCACTTCAACTCTC
TTCACATCGTCAACACTTACGGGGCCTTCGGAAGCATCACAAGGAGCGGGCGGAGGTGA
TCCTGCAGGGCACAGCCAGCTCCAACGCCAGCGCCCCGATGCCATGTGGGAGGACTACG
AGTTCAAGTGCAAGCCAGGTGACCCAGCAGACGGCCTGCCTCATCTCCCGTACCACT
ACCGCTGGACTGGCTGATGTGGTTCCGCGCCTTCCAGACCTACGAGCACAACTGGA
TCATCCACTGGCTGGCAAGCTCTGGCCAGCGACCGGAGGCTTGTCCCTGCTGGCAC
ACAACCCCTTCGCGGGCAGGCCCCCGCCAGGTGGTCCGAGGAGAGCACTACAGGTACA
AGTTGAGCCGCTCTGGGGGAGGCACGCGCGGAGGGCAAGTGGTGGTGGCGGAAGAGGA
TCGGAGCCTACTTCCCTCCGCTCAGCCTGGAGGAGCTGAGGCCCTACTTCAGGACCGTG
GGTGGCCTCTGCCGGGCCCTCTAGACGTGCACCAGAAATAAAGGCGAAGACCCAGCCC
CTCGCGGCTCAGCAACGTTTGCCTTCCCTGCGCCAGCCCAAGCTGGGCATCGCCAAG
AGAGACBTGGAGAGGAGAGCGGTGGGACCCAGCCCCAGCACGGGGTCCAGGGTGGGGT
CTGTTGTACATACTGTGGCGCTCCAGGCCCTGCCACCTGGGGCCCCACATCCAGGC
CAACCTTGTCCAGGCGCCAGGGGCTCTGATCTCCCATCCATCCACCCTCTCCAGGA
GGCCAGCCTGGGGCTGTGCCGCCACAGGAGTTGAGACAAATGGCAATCCTGACACCTTC
CTCCACTACAGCCCTGACCATAGACCCAGCCAGGTAGCTCTGGGGTCTCTAGCGTCCA
GGCCTGGTTTCTGTTCCCTCTCAATGGTGTGTTCCAGCCAGGTCTTGACCCTCAGAG
CCAAGTCCCTGTACGTCTGGGGCAGCCAAACCTCGCCCCAGGGACCTGGACACGCC
CGCCAGGATGTGGGGTTGGATGGGCCATTTCTGTCTATCCCTCATCTCCACCCCGC
CACAGCCTACAGCATCCACACATGCAGGCACACAGCCTGTGCACACATGTGTTCTT
GGCCGGTTTCTATCCCCCATGACTGGTGTCTGTGAGGTGCAGATGGACACAGCGCAC
CCAGACCTCCACCAGGCTGTGACCTCGCTGCCCTGTGAGGCTTGACAAGGCCCTCAAT
CGGAGGACAGCCGGCTGCACACTTTCATCATCGTCGGACAAACAGCGTCTACTGCACA
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ACCACTTACCAGCTTACTCG

FIGURE 69A

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA334818
><subunit 1 of 1, 567 aa, 1 stop
><MW: 64874, pI: 9.45, NX(S/T): 3

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AFVYFVAFLVAFHQKQLIGDRGLPCRVLKDFQQYFQDRTSWEVFSYMP TILWLM DWS
DMNSNLDLLALLGLGISSFLITGCANMLLMAALWGLYMSLVNVGHVWYSFGWESQLEET
GFLGIFLCPLWLSRLPQHTPTSRIVLWGPRWLI FRIMLGAGLIKIRGDRCDLTCMDF
HYETQMPNPVAYYLLHSPWWFHRFETLSNHFI ELLVPPFFLFLGRRACI IHGVLQILFQA
VLIVSGNLSFLNWLTMVPSLACFDDATLGFLFPSPGPGSLKDRVLQMQRDIRGARPEPRFG
SVVRRANVSLGVLLAWLSVPVVLNLLSSRQVMNTHFNSLHIVNTYGAFGSITKERA EVI
LQGTASSNASAPDAMWEDYEFKCKPGDPSRRPCLISPHYRLDWLMWFAAFQTYEHNDWI
IHLAGKLLASDAEALSLLAHNPFAGRPPPRWVRGEHYRYKFSRPGGRHAAEGKWWVRKRI
GAYFPPLSLEELRPYFRDRGWPLPGPL

Transmembrane domain.

Amino acids 51-71, 124-144, 175-195, 205-225, 272-292, 295-315,
320-340, 365-385.

Protein of unknown function (DUF1222) domain.

Amino acids 362-549.

N-glycosylation site.

Amino acids 307-310, 368-371, 428-431.

Glycosaminoglycan attachment site.

Amino acids 334-337.

cAMP- and cGMP-dependent protein kinase phosphorylation site.

Amino acids 17-20.

Protein kinase C phosphorylation site.

Amino acids 14-16, 202-204, 338-340, 388-390, 449-451.

Casein kinase II phosphorylation site.

Amino acids 23-26, 102-105, 124-127, 236-239, 338-341, 430-433,
490-493, 548-551.

Tyrosine kinase phosphorylation site.

Amino acids 101-109.

FIGURE 69B

N-myristoylation site.

Amino acids 83-88, 133-138, 156-161, 372-377, 407-412, 423-428, 525-530.

Amidation site.

Amino acids 283-286.

Prokaryotic membrane lipoprotein lipid attachment site.

Amino acids 135-145.

Cell attachment sequence.

Amino acids 227-229.

FIGURE 70

getseq sst.DNA257501

GGCACGAGGAGAAGACTTTGGTGGGGTAGTCTCGGGGCAGCTCAGCGGCCCGCTGTGCC
GTTTCTGGCCTCGCTCGCAGCTTGCACGTCGAGACTCGTAGGCCGCACCGTAGGGCGAGC
GTGCGGGTTCGCGCCGCGGGCCCTCGGGGTCTGGGCCAGCCGCGAGCCTCTTCTACCGC
GGCCGGTTGGGAGTCGCCGCGAGATGCCAGCCTCCGGGCCGCCCGCCGCTATGCCCCCA
CTAACGGGGACTTCACCTTTGTCTCCTCAGCAGACGCGGAAGATCTCAGTGGTTCAATAG
CATCCCCAGATGTCAAATTAATCTTGGTGGAGATTTTATCAAAGAATCTACAGCTACTA
CATTTCTGAGACAAAGAGGTATGGCTGGCTTCTGGAAGTGAAGATGATGATCCTGAAG
ATAACAAGCCACTCTTGGAGAATGGACATGATCTAAAGGATATTTACTACAAAATCC
GATGTGTTTTGATGCCAATGCCATCACTGGTTTTAATAGACAAGTGGTGAGAGACAATC
CTGACTTTTGGGGTCTCTGGCTGTTGTTCTTTTCTTTCCATGATATCATTATATGGAC
AGTTTAGGGTGGTCTCATGGATTATAACCATTTGGATATTTGGTTCACTAACAAATTTCT
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ATTCATTACTTCTCTCATTGTAATAGCCCTGTACTTTTGGTGGTTGGATCATTTGAAG
TGGTGTCTACACTTATAAACTGTTTGGTGTGTTTTGGGCTGCCTACAGTGTCTGCTTCAT
TGTTAGTGGGTGAAGAATCAAGACC AAAAGCCTCTTCTGATTTATCCAATCTTTTTAT
TATACATTTATTTTTTGTCTTATATACTGGTGTG IGATCCAAGTTATACATGAATAGAA
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CTGTTGCTGCAAAATTTACATGTTCCAGATGGAAAGGGAAGTCTAAGCGCTTTTTAAAA
CAATTTTTTTTTGTATTTAATTAAGCAATTCAGTTATCTGGGATTTTGGGTGAGAAAT
TTAAATCTGTTTGATTCTCCATATCCAGTGAATAAAAATACAAAAGCATTGTGTTTTTA
AGATTGTGTCGATATTCACCTAAAAACTTGTGCCAAAAGCACCTGGATTGGTAATTATAT
TTCACTTAAAGGGTAAATTTGACAATATCTTGATAATCAAAGTGCAATTTTTTTCTTCA
AAATGTTTTCTCCAGCATCACAGATCCTGCAGATATATAATTTATATTTATACATATATAT
TTATGAAATAAATCTTACTCAAAAATATATTTCTGATAAACATTAAGATATTAATCTG
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TAATAACTACTAAAACCTGATTTTTAATAGTTGCTGATATATATTTGGTTTGTGGGTAT
ACTTTTCAAACCATTTTGAATGTCAAACATCTGATTTAAAGTTCTGTTTATCTTTC
TGACCAAAGGAGCAAGAGGTATAATGGATATGGCATTCAATAAAATCTTACTATGTACA
AAAACAGTAATATTTACAGCATCAGTAAATATTTTTAAGTGGTACTTCTAAATCATAAAA
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AATAAAATACTTCCAGTTGTGAAAAAAAAAAAAAAAAAAAA

FIGURE 71

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GWLLEVEDDDPEDNKPLLEELDIDLKDIYYKIRCVLMPMPSLGFNRQVVRDNPDFWGPLA
VVLFFSMISLYGQFRVSVIITIWIFGSLTIFLLARVLGGEVAYGQVLGVIGYSLLPLIV
IAPVLLVVGSEFEVSTLIKLFVFWAAYSAASLLVGEBFKTKKPLLIYPIFLLYIYFSL
```

Transmembrane domain.

Amino acids 115-135, 136-156, 170-190, 186-206, 224-243.

Yip1 domain.

Amino acids 81-226.

Protein kinase C phosphorylation site.

Amino acids 221-223.

Casein kinase II phosphorylation site.

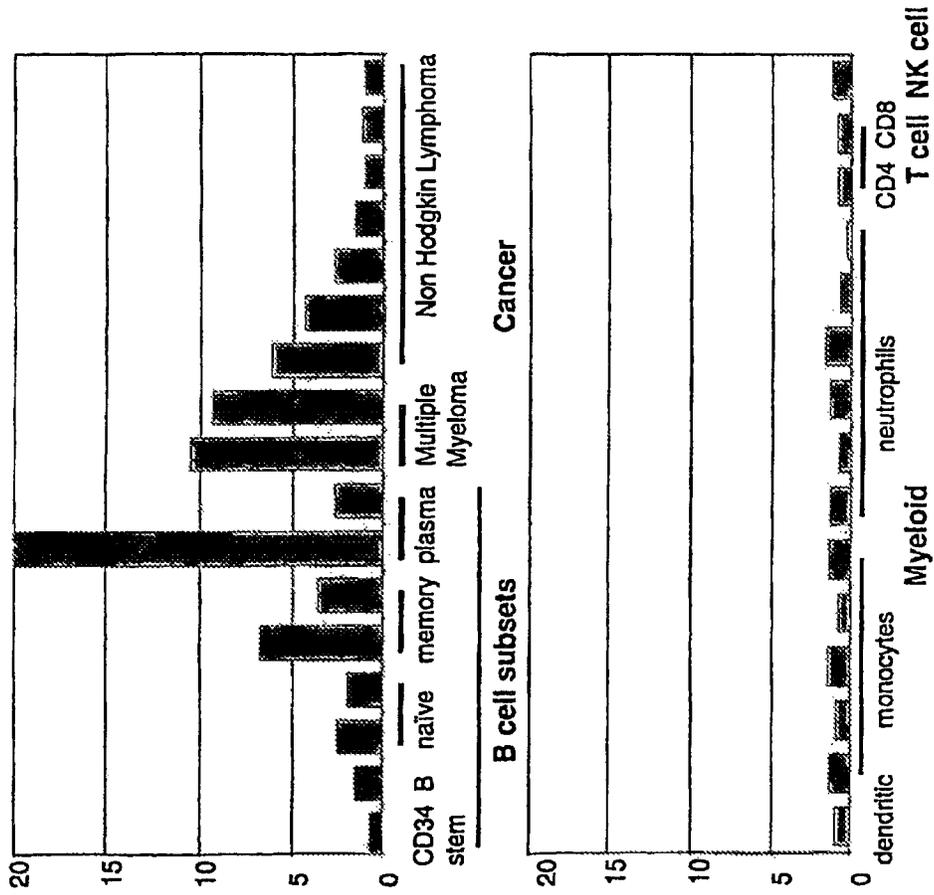
Amino acids 13-16, 21-24.

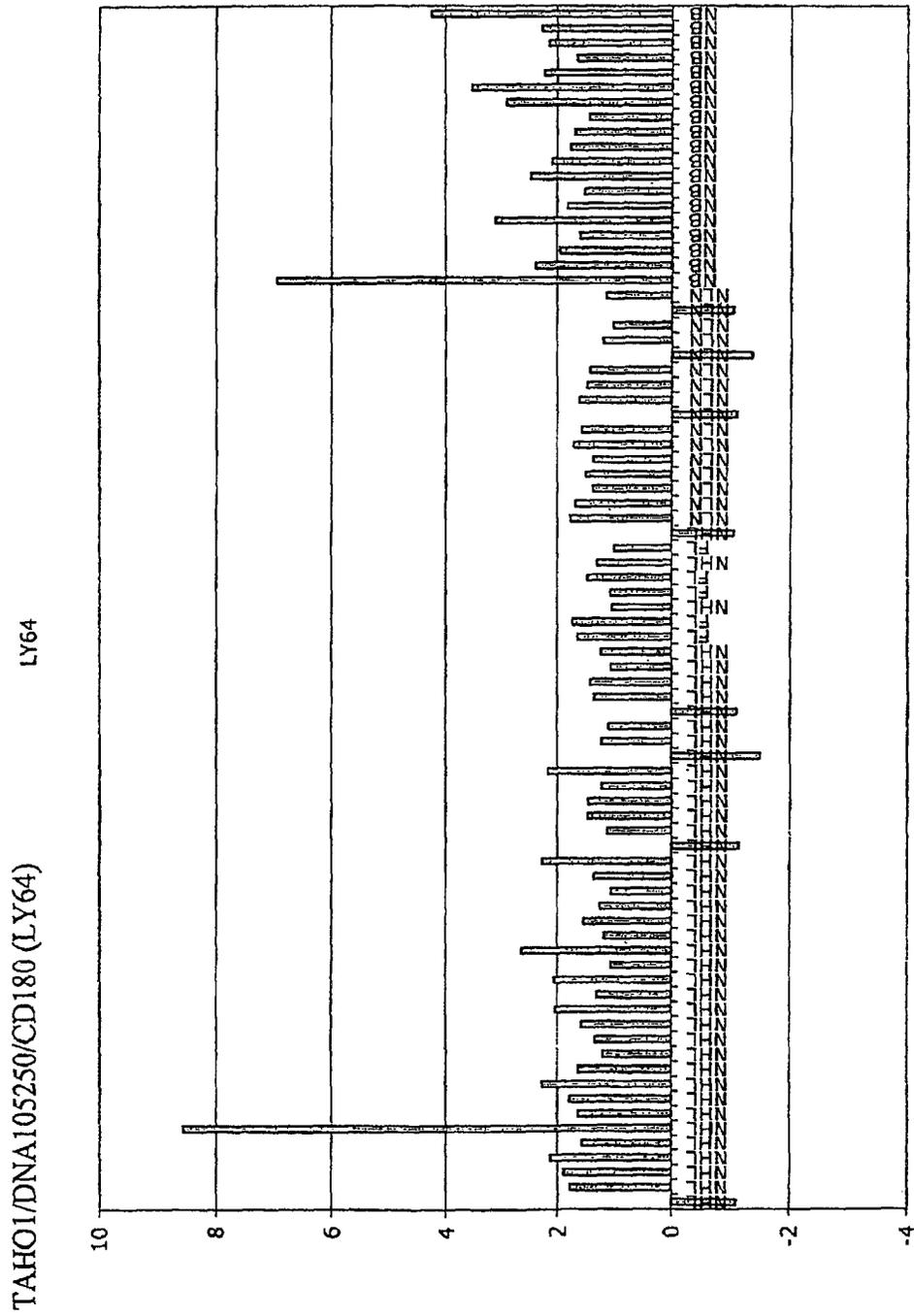
N-myristoylation site.

Amino acids 159-164, 165-170, 202-207.

FIGURE 72

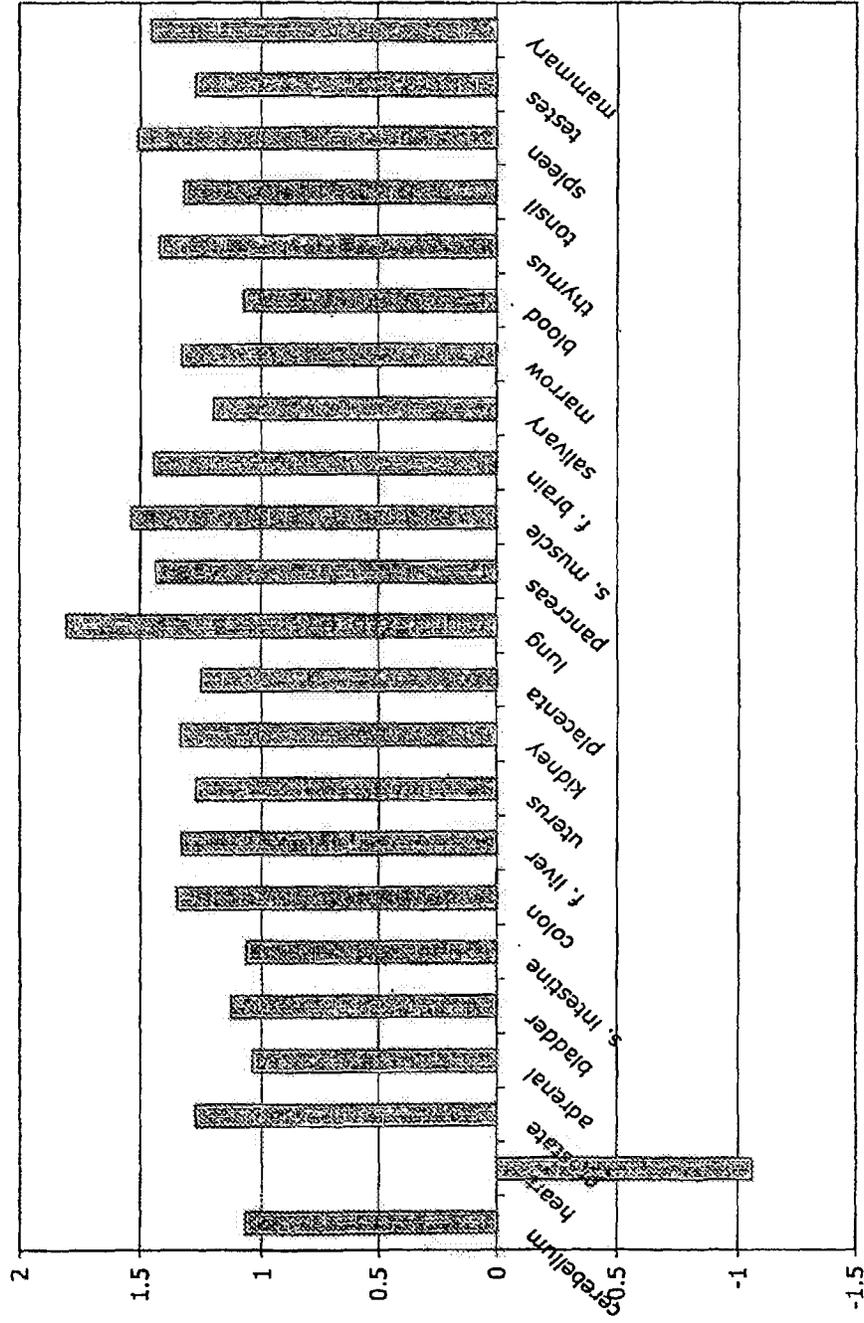
TAHO15/DNA58721/NAG14





LY64

TAHO1/DNAI05250/CD180 (LY64)

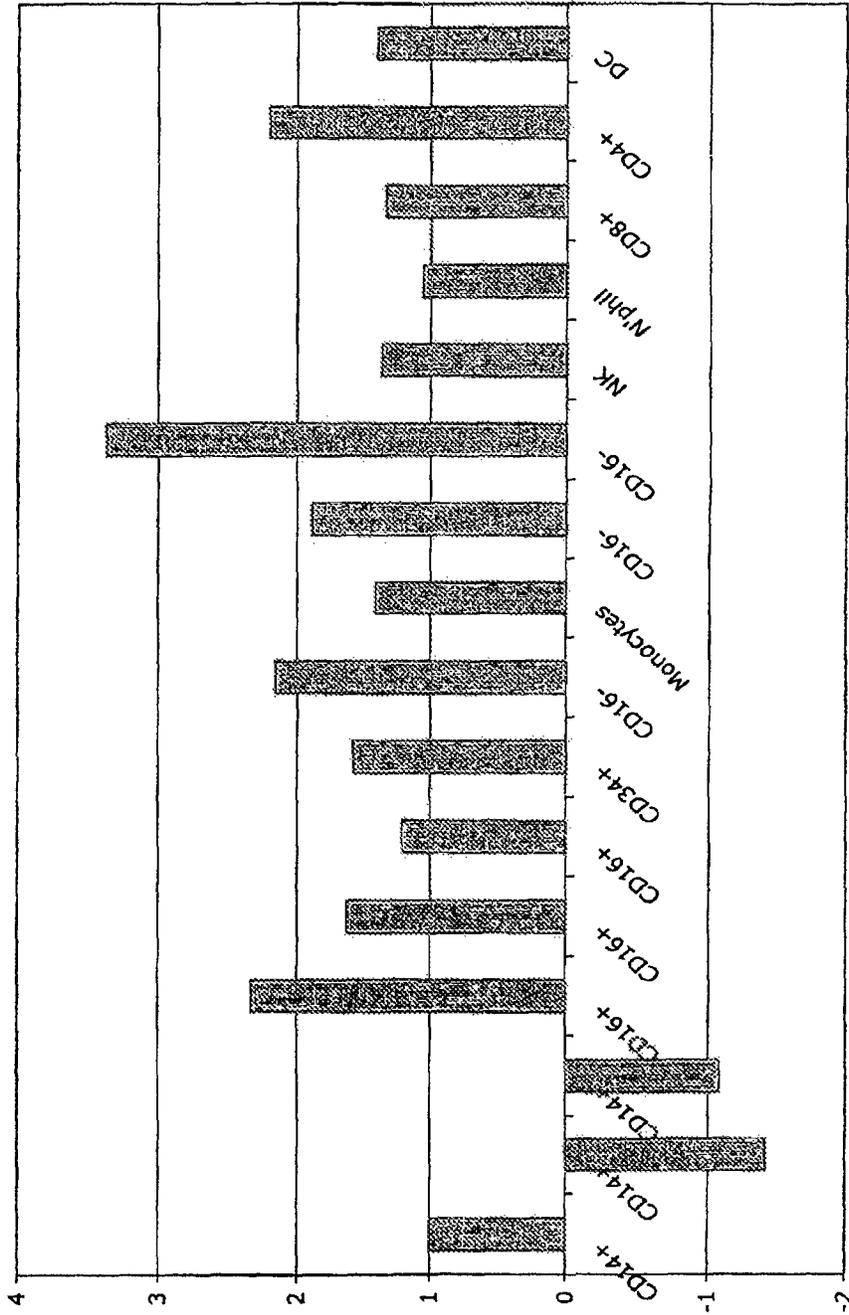


samples

FIGURE 73B

TAHO1/DNA105250/CD180 (LY64)

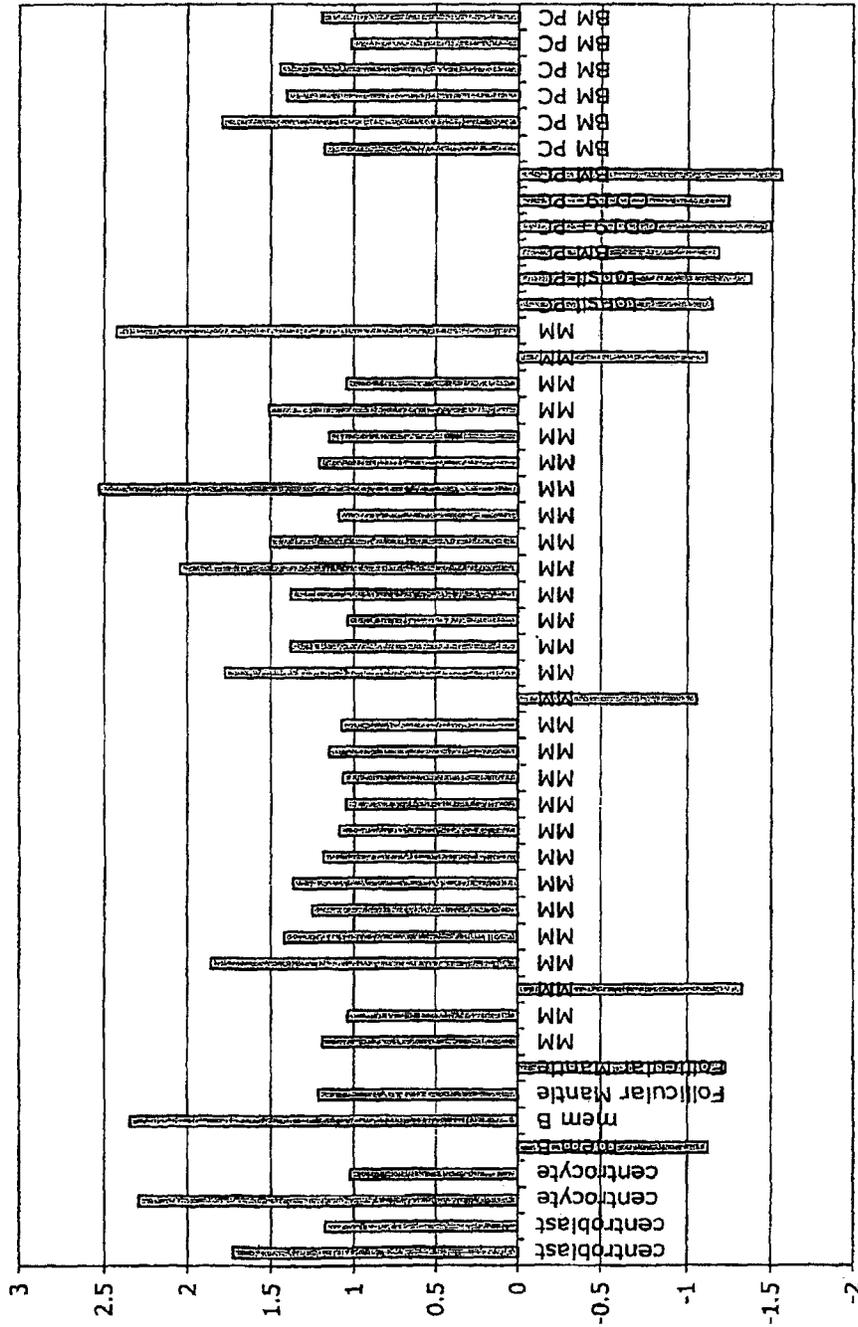
LY64



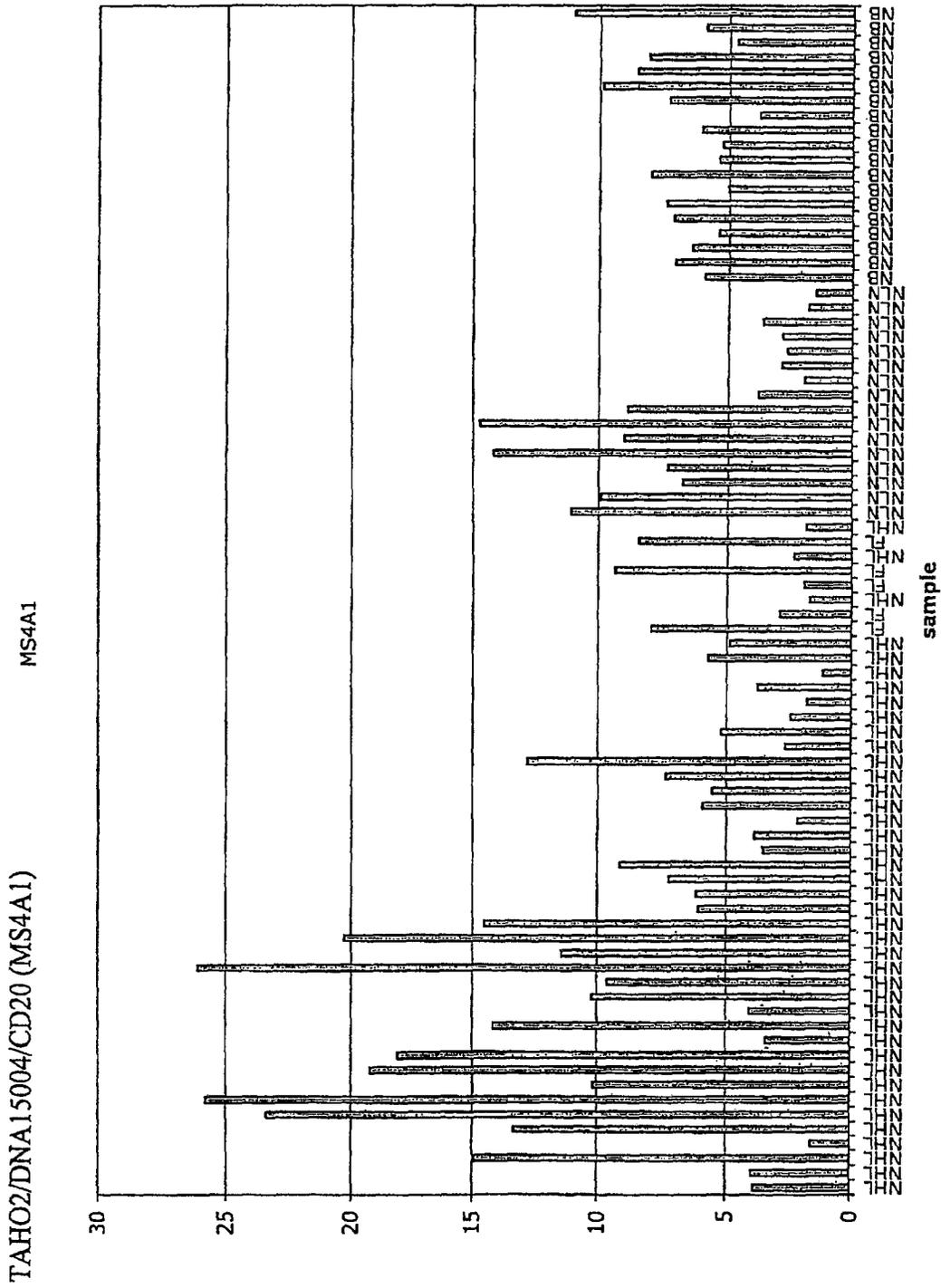
sample
FIGURE 73C

TAHOI/DNAI05250/CD180 (LY64)

LY64



sample
FIGURE 73D



TAHO2/DNA15004/CD20 (MS4A1)

MS4A1

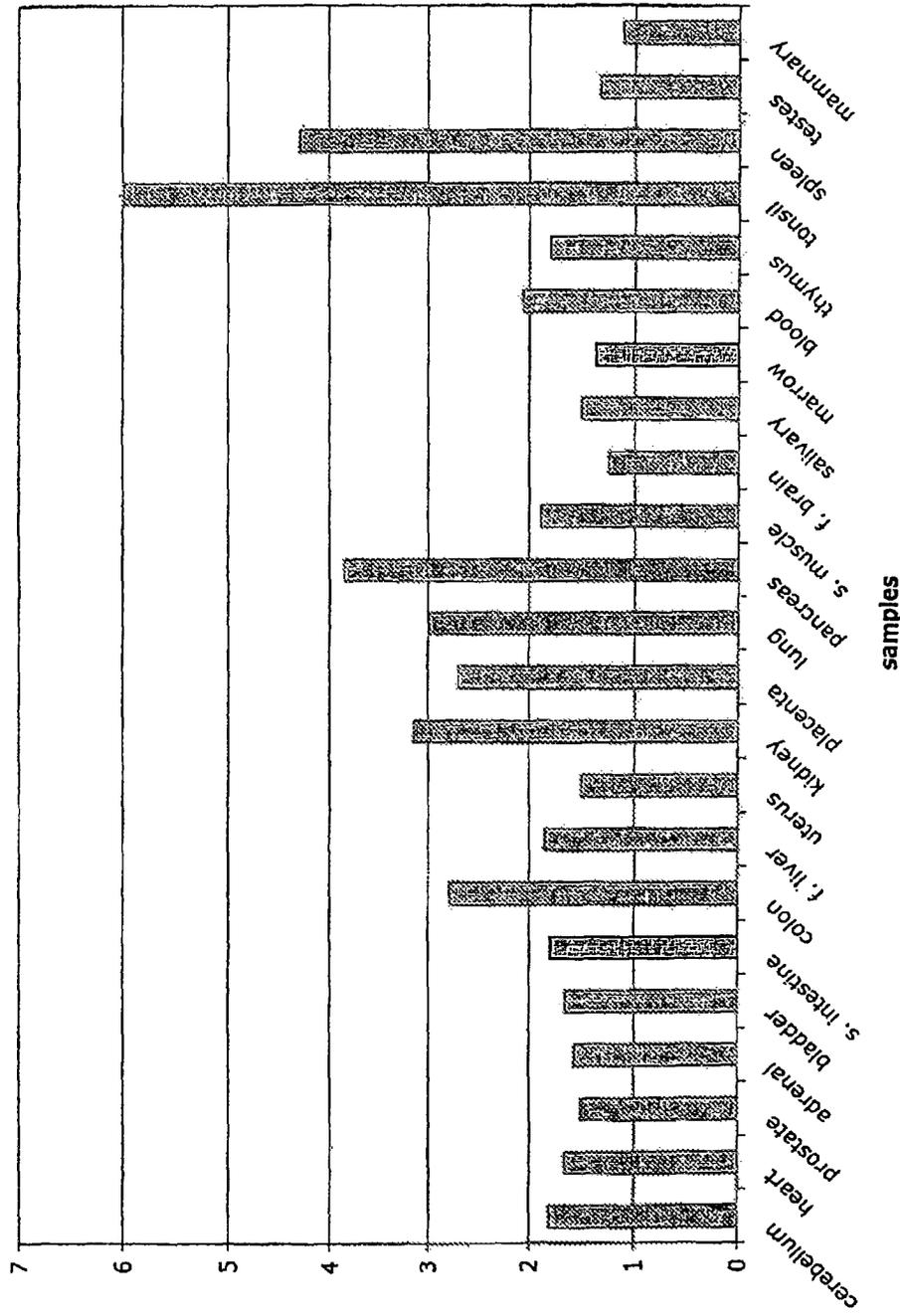


FIGURE 74B

TAHO2/DNA15004/CD20 (MS4A1)
MS4A1

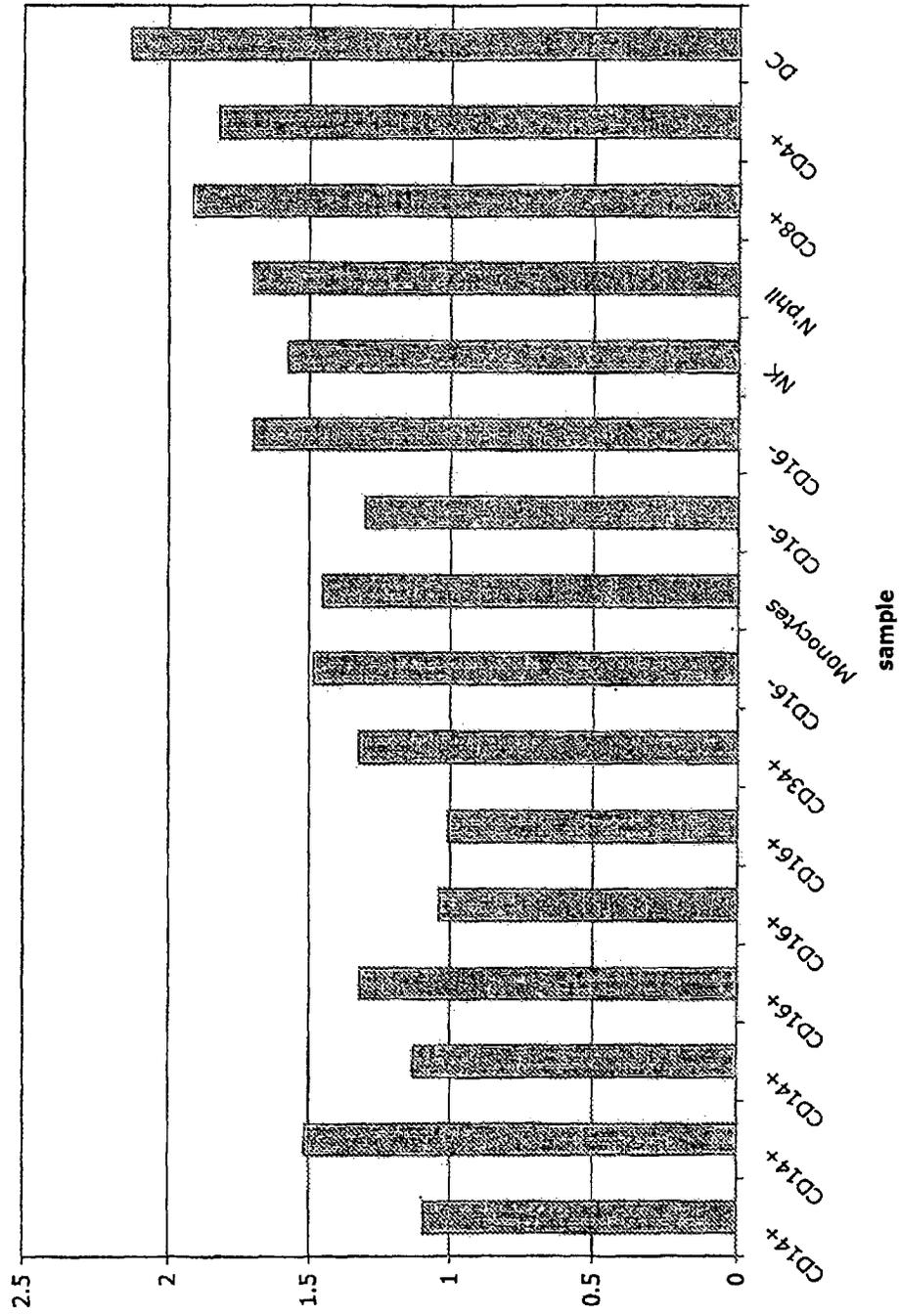
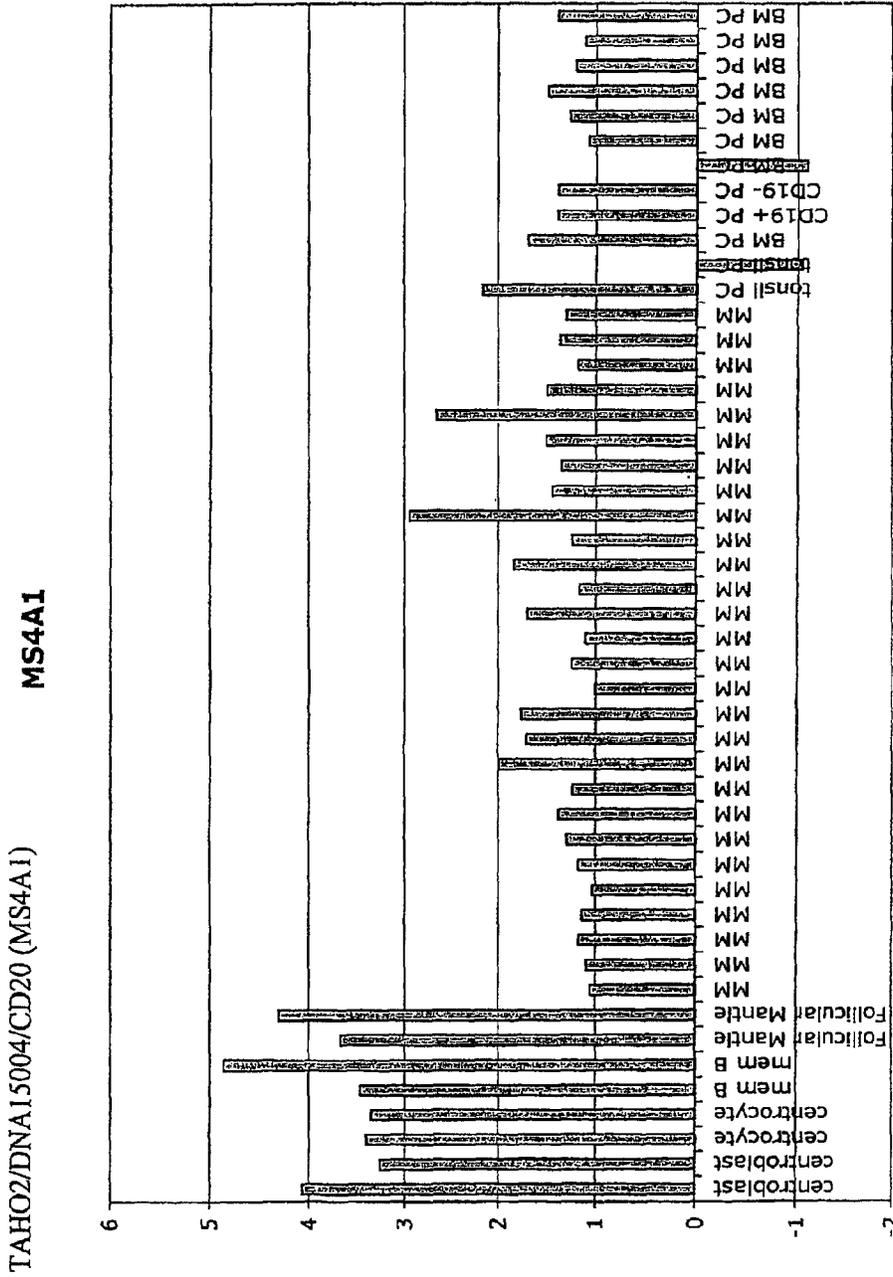


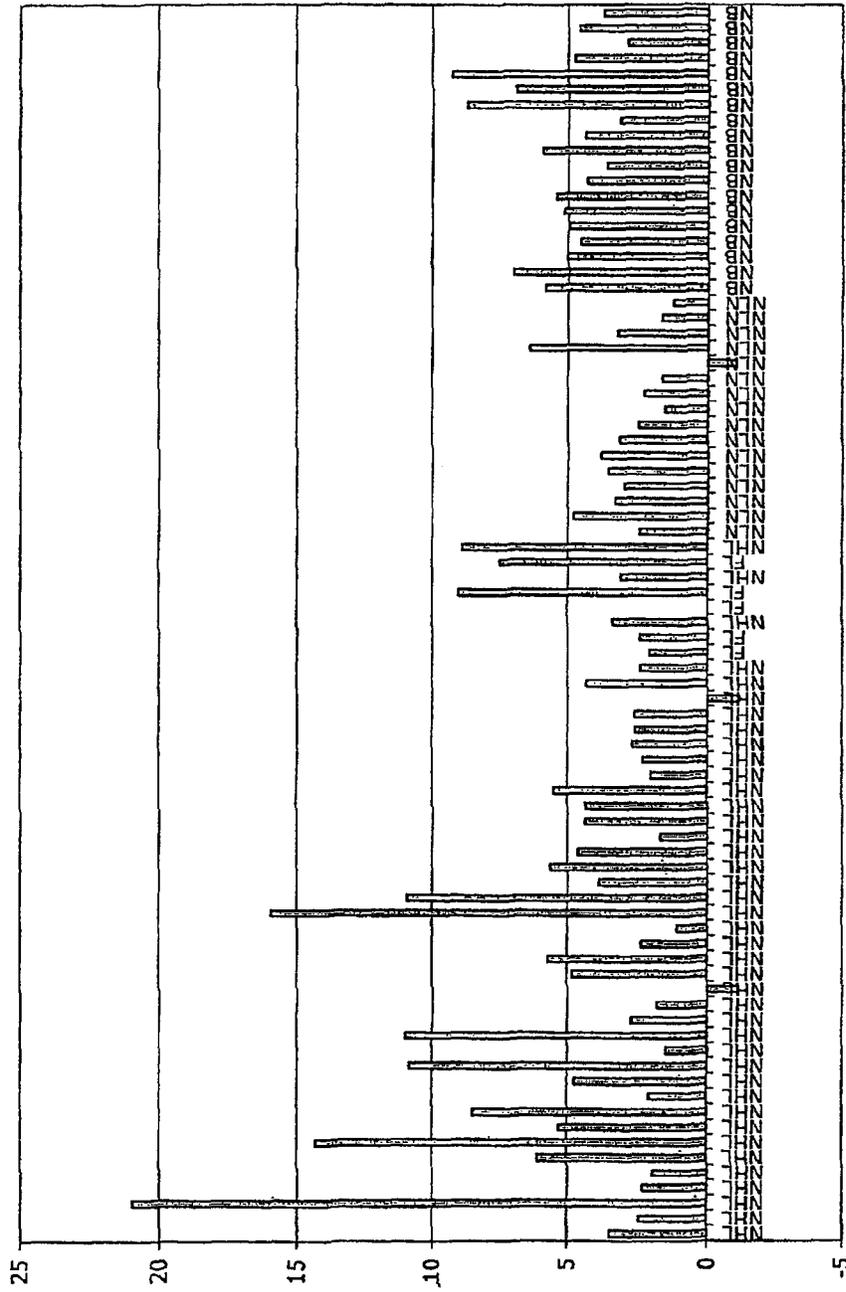
FIGURE 74C



sample
FIGURE 74D

TAHO3/DNA182432/FcRH2 (SPAP1)

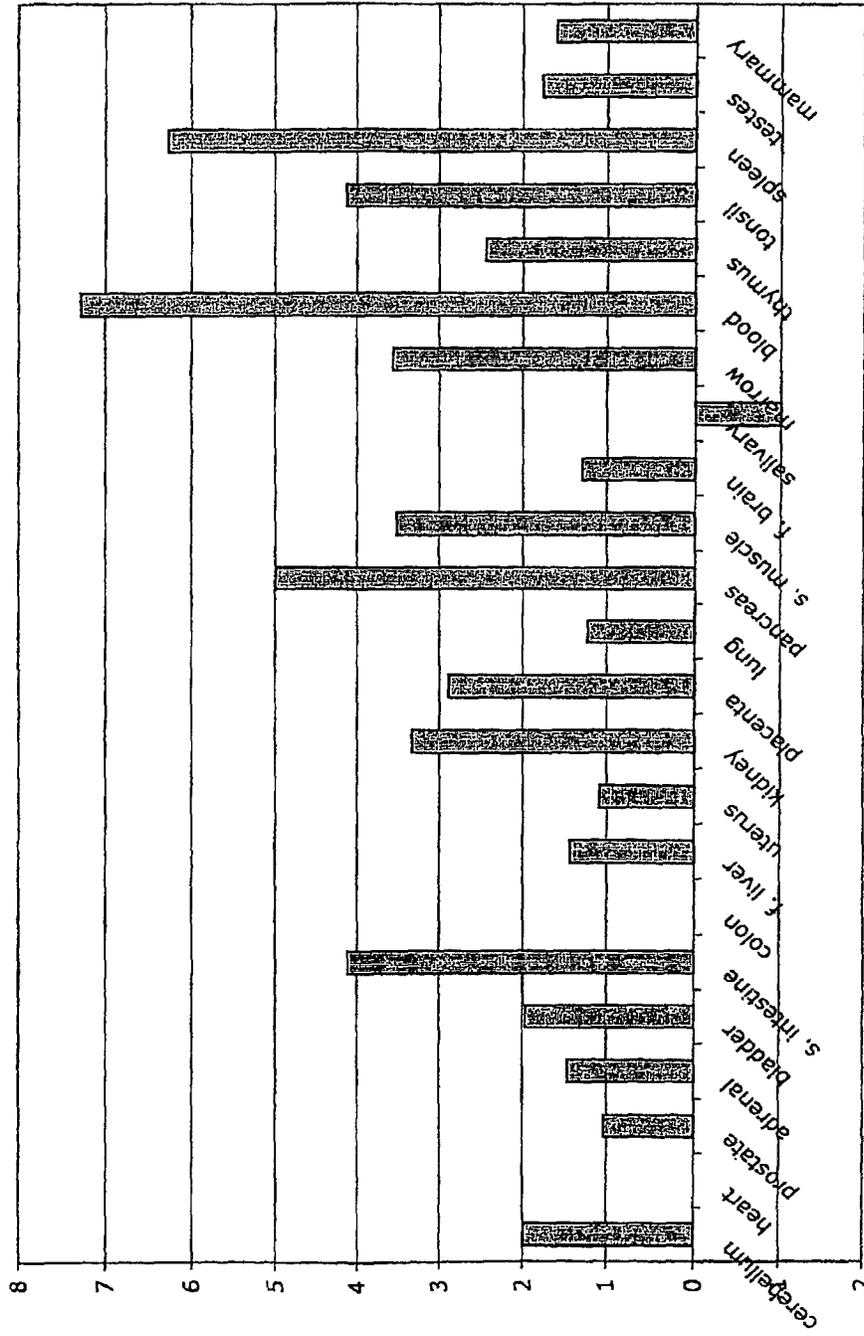
SPAP1



sample

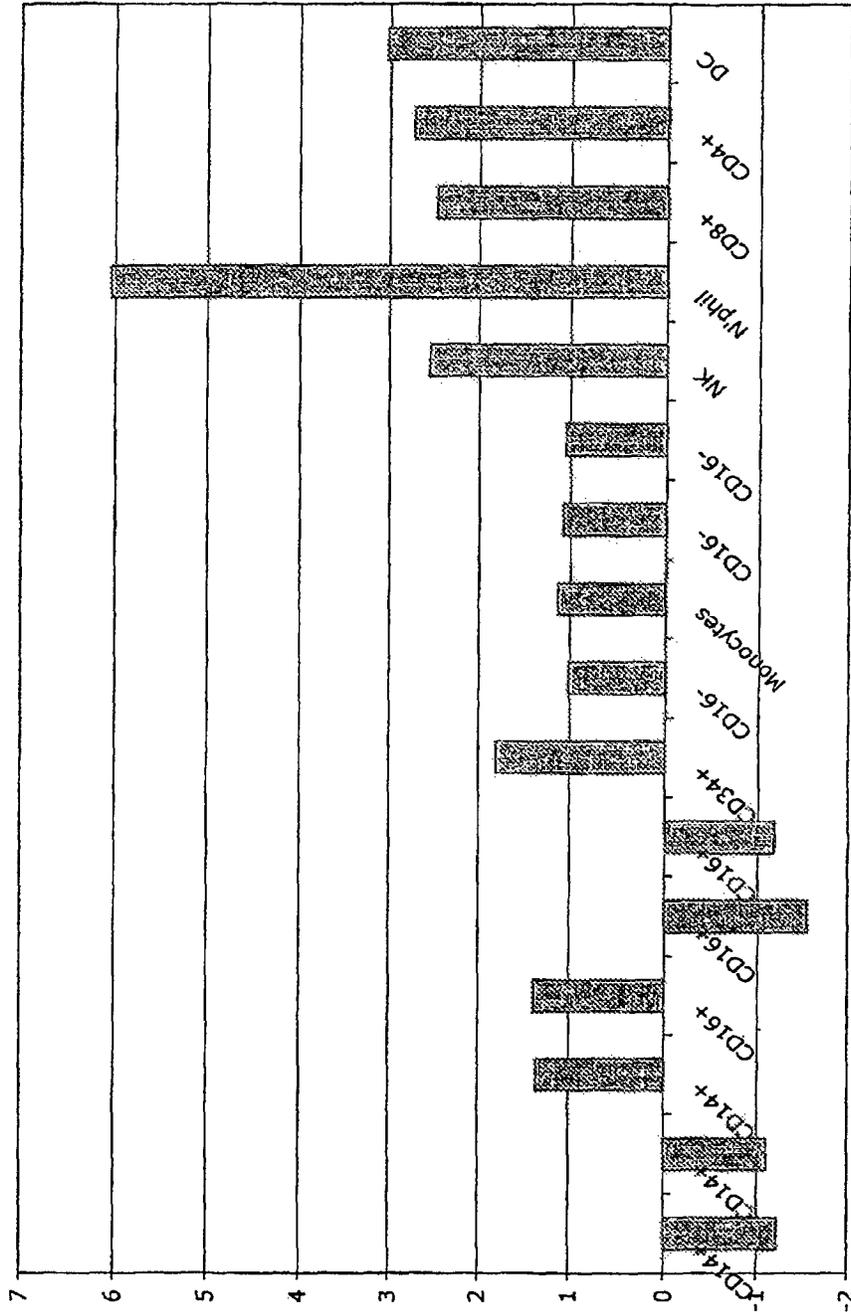
FIGURE 75A

TAHO3/DNA182432/FcRH2 (SPAP1) **SPAP1**



samples
FIGURE 75B

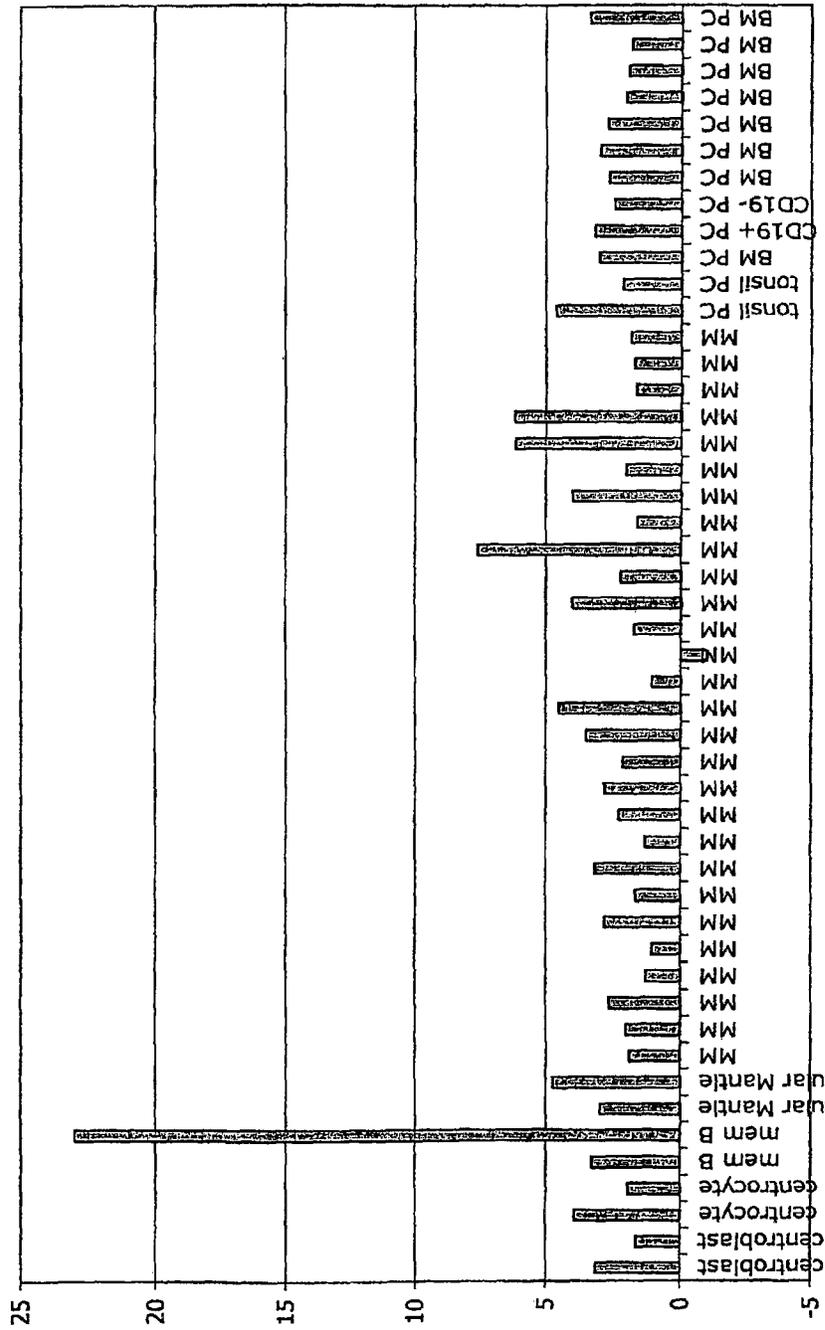
TAHO3/DNA182432/FcRH2 (SPAP1)
SPAP1



sample
FIGURE 75C

TAHO3/DNAI82432/FcRH2 (SPAP1)

SPAP1



sample

FIGURE 75D

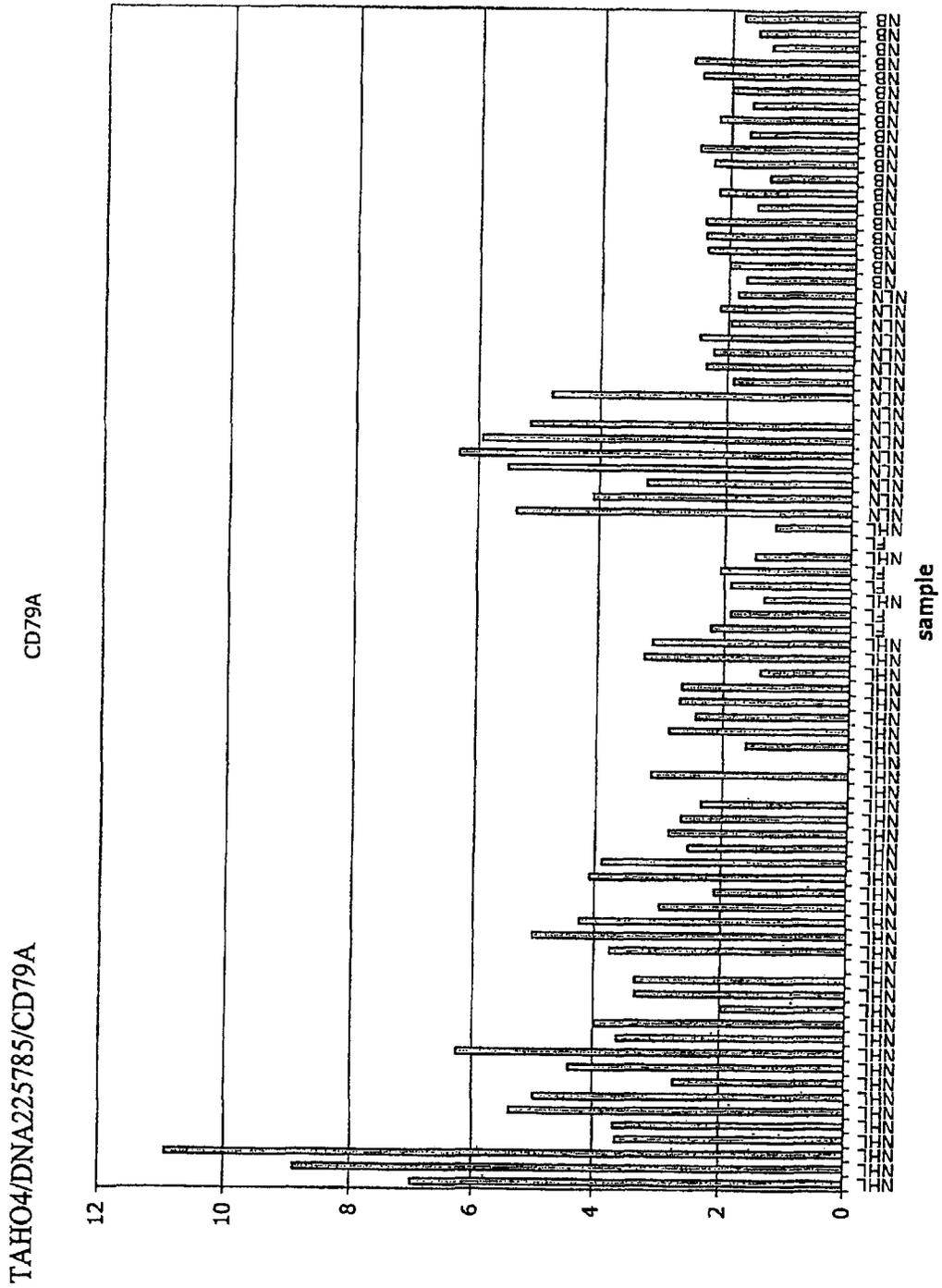
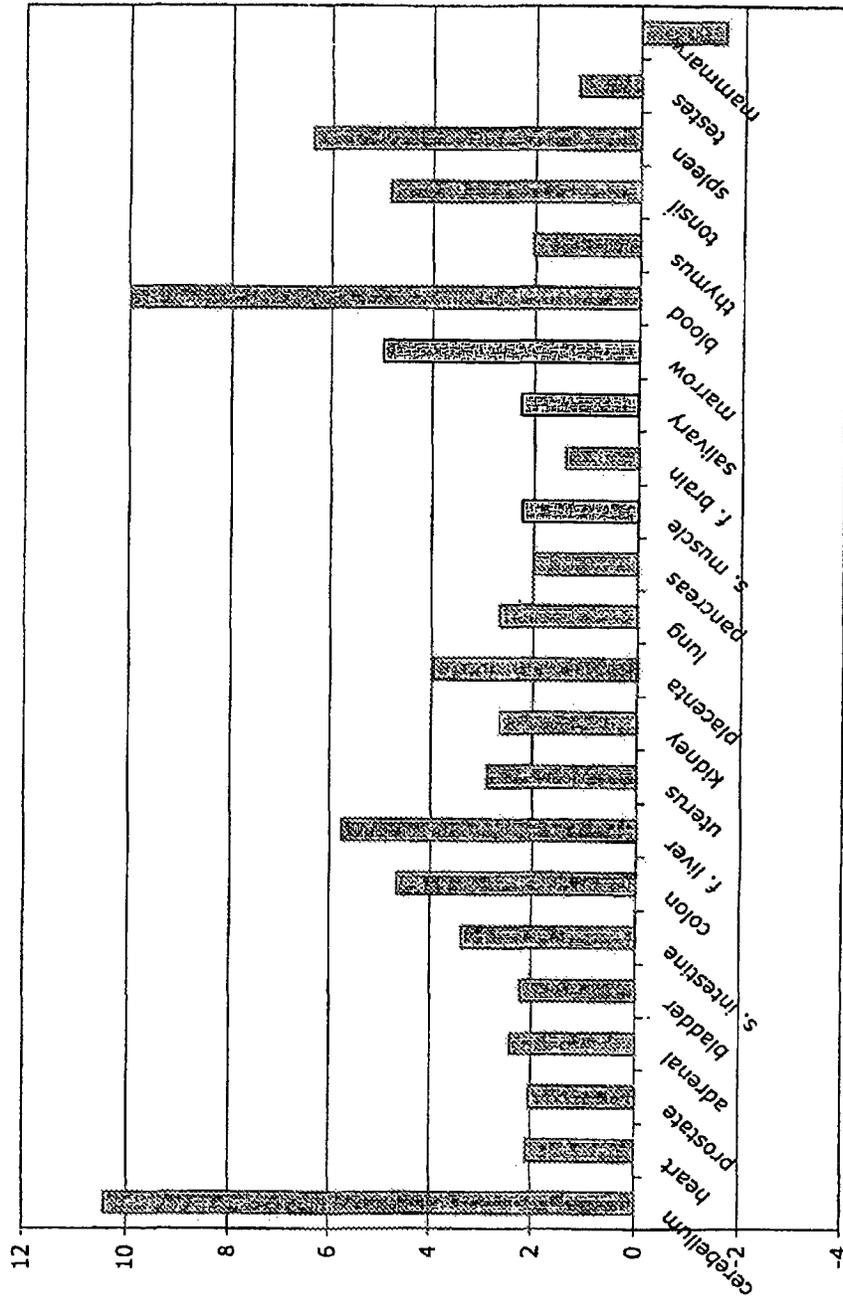


FIGURE 76A

TAHO4/DNA225785/CD79A

CD79A



samples
FIGURE 76B

CD79A

TAHO4/DNA225785/CD79A

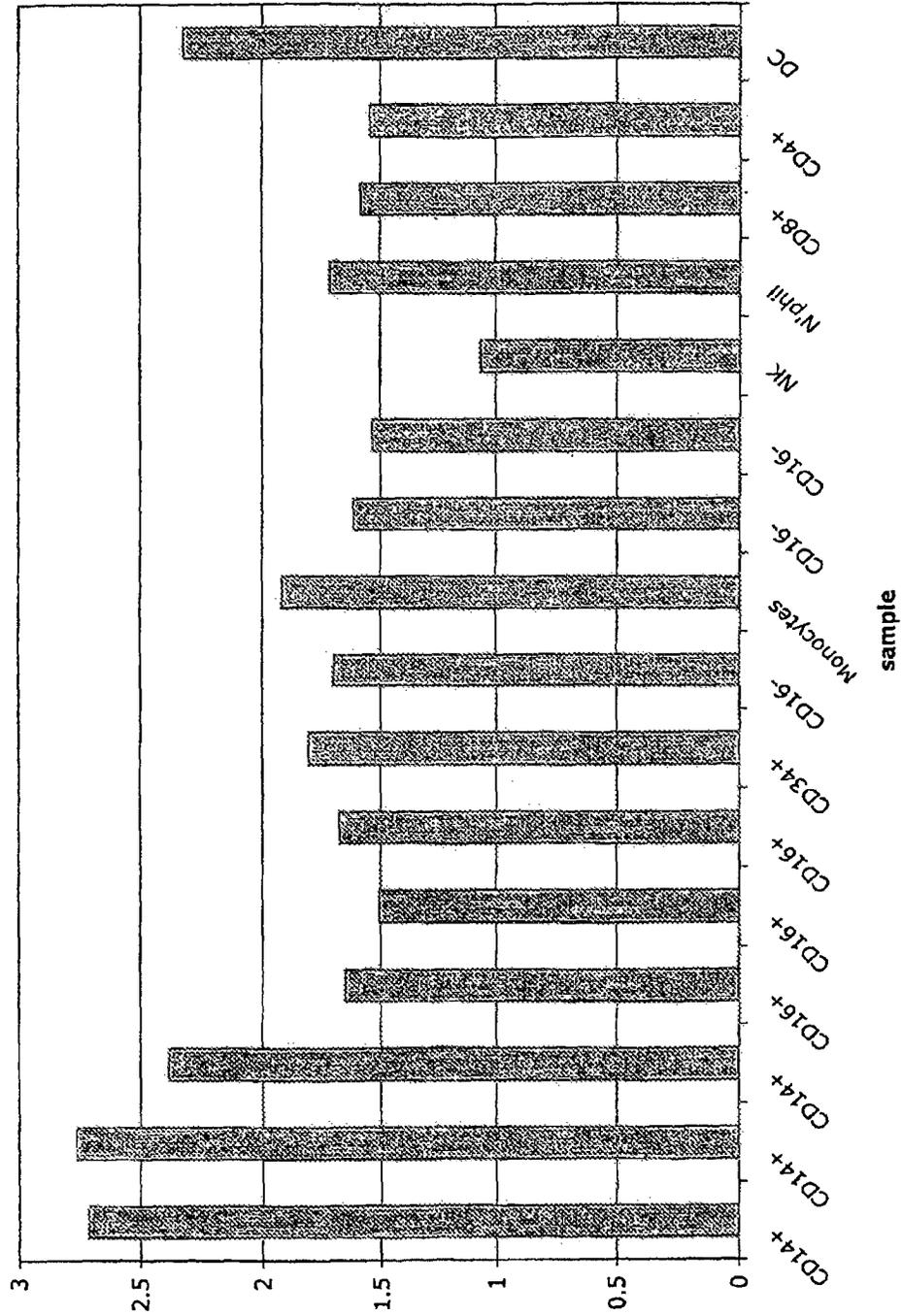
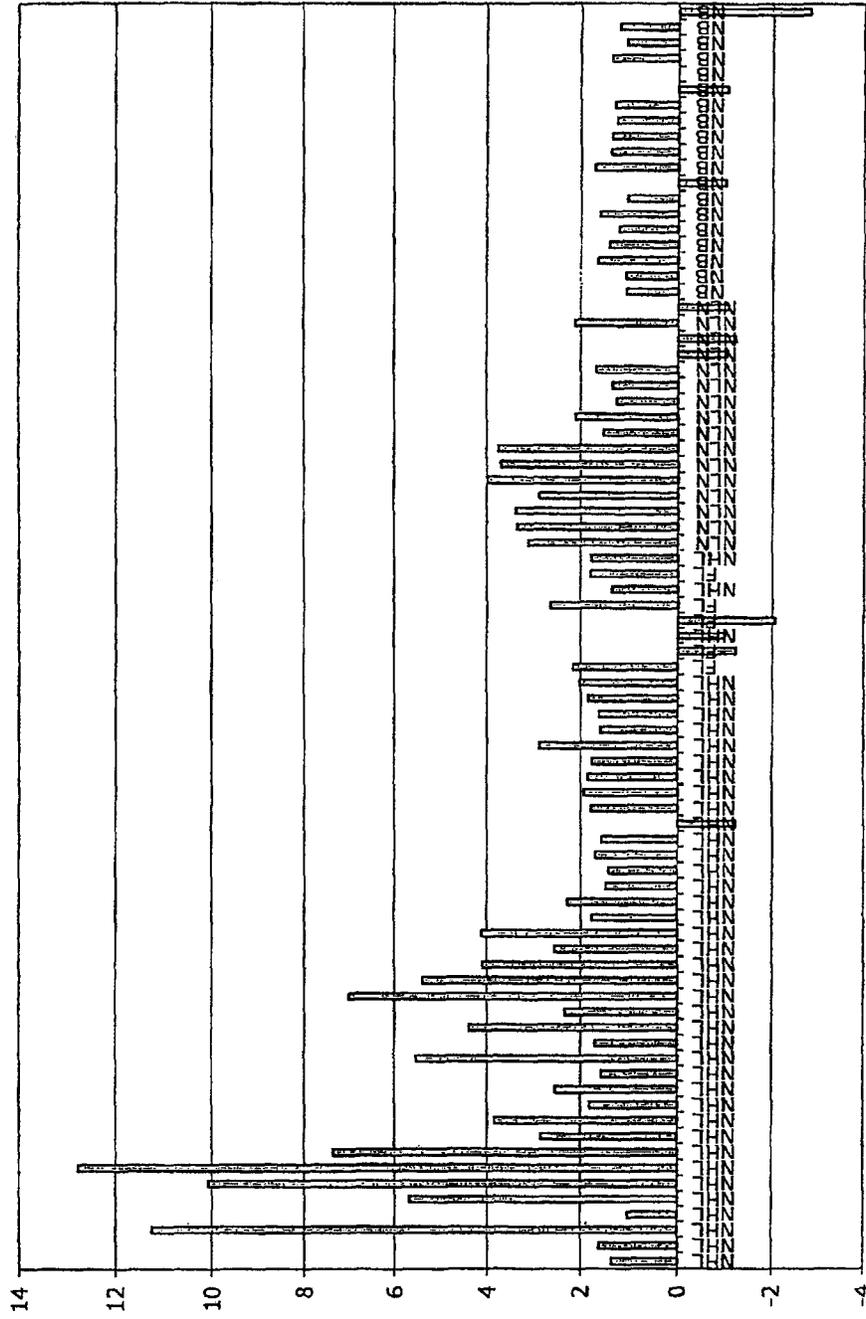


FIGURE 76C

TAHO5/DNA225786/CD79B

CD79B

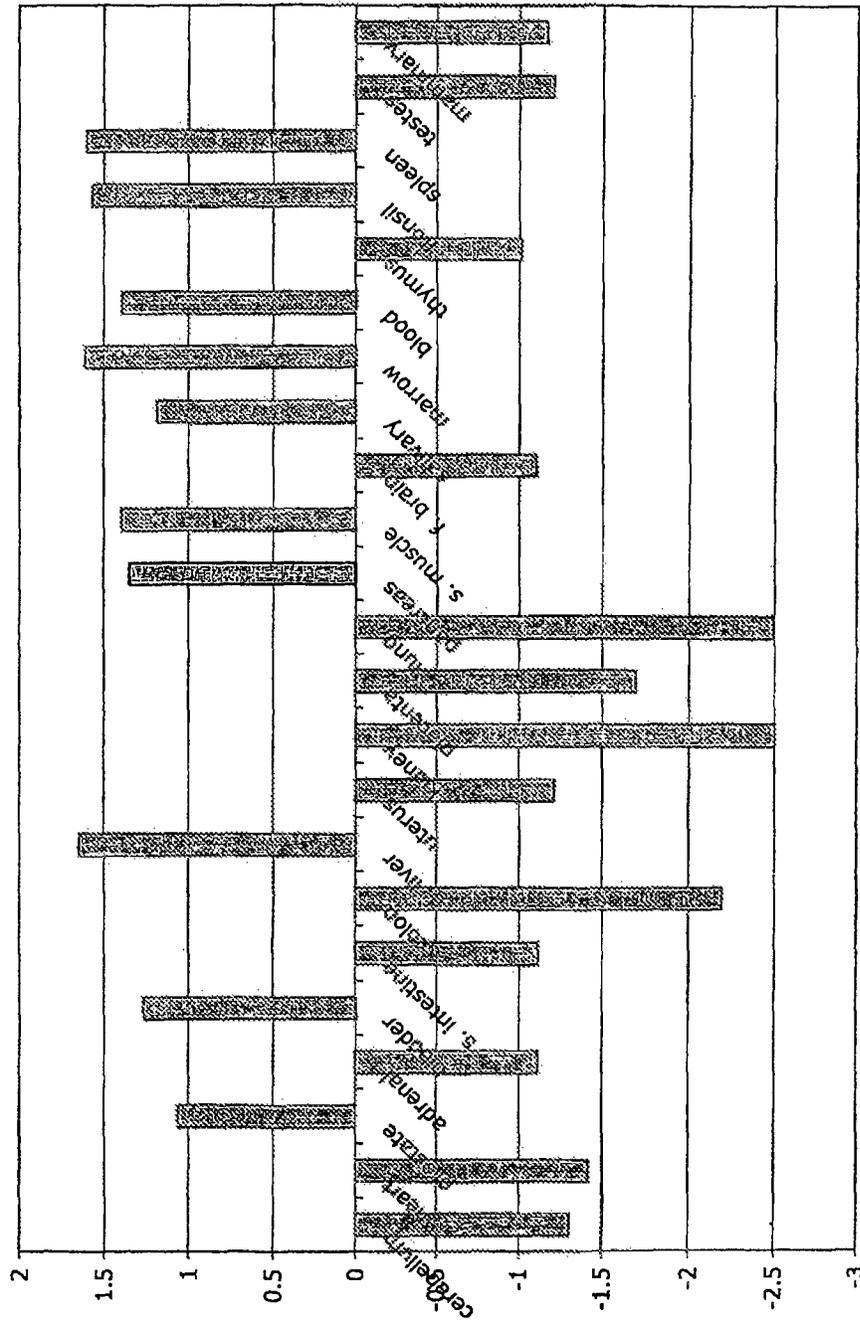


sample

FIGURE 77A

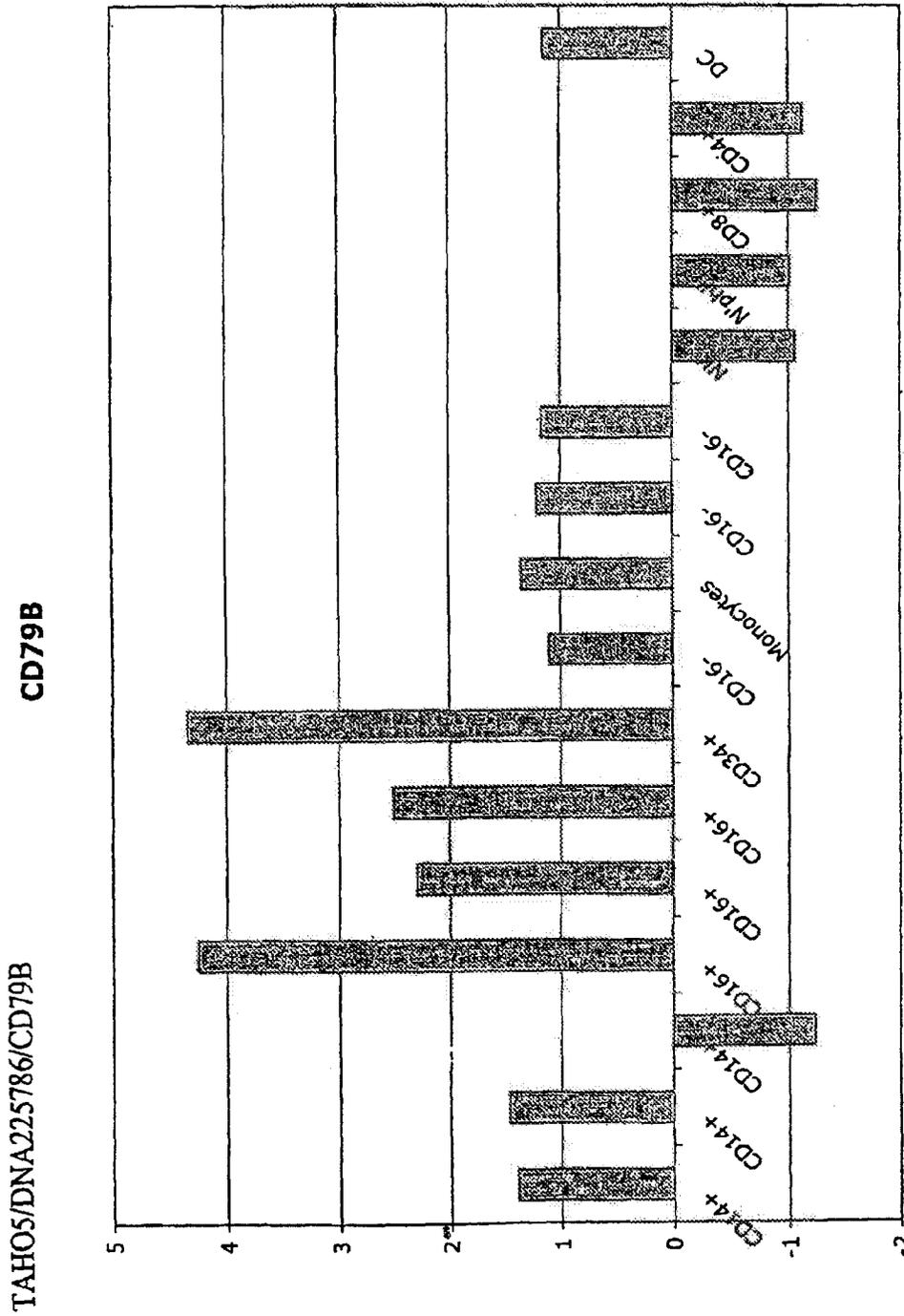
TAHO5/DNA225786/CD79B

CD79B



samples

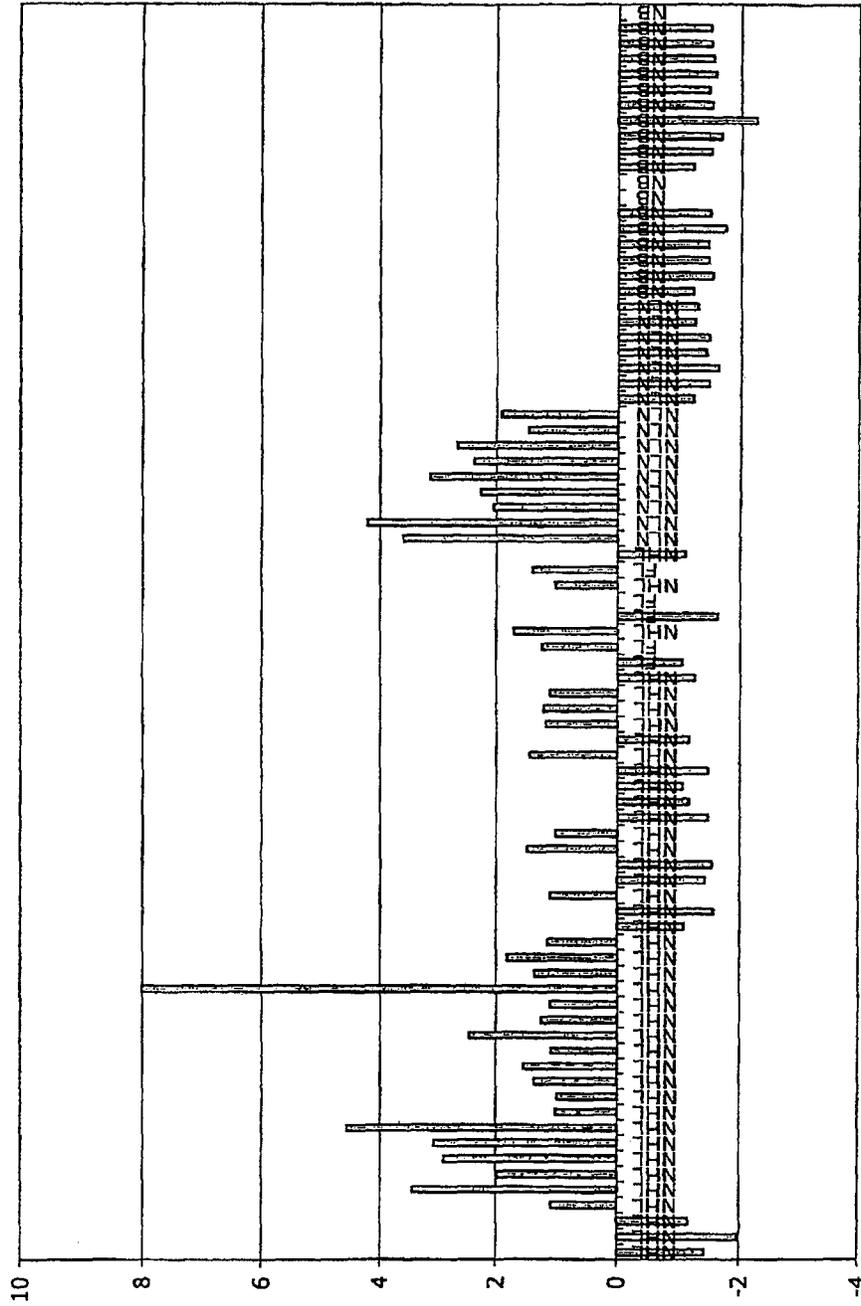
FIGURE 77B



sample
FIGURE 77C

TAHO6/DNA22.5875/CD21 (CR2)

CR2

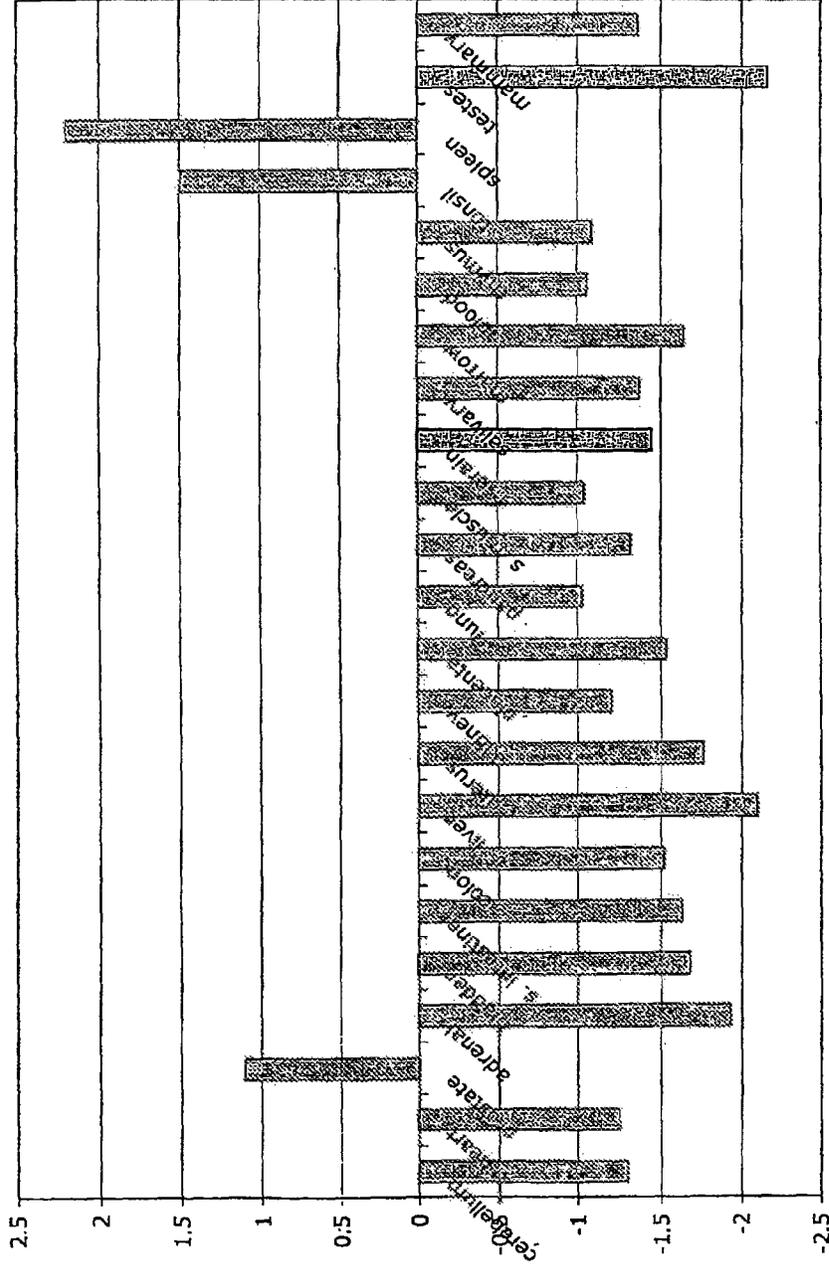


sample

FIGURE 78A

TAH06/DNA225875/CD21 (CR2)

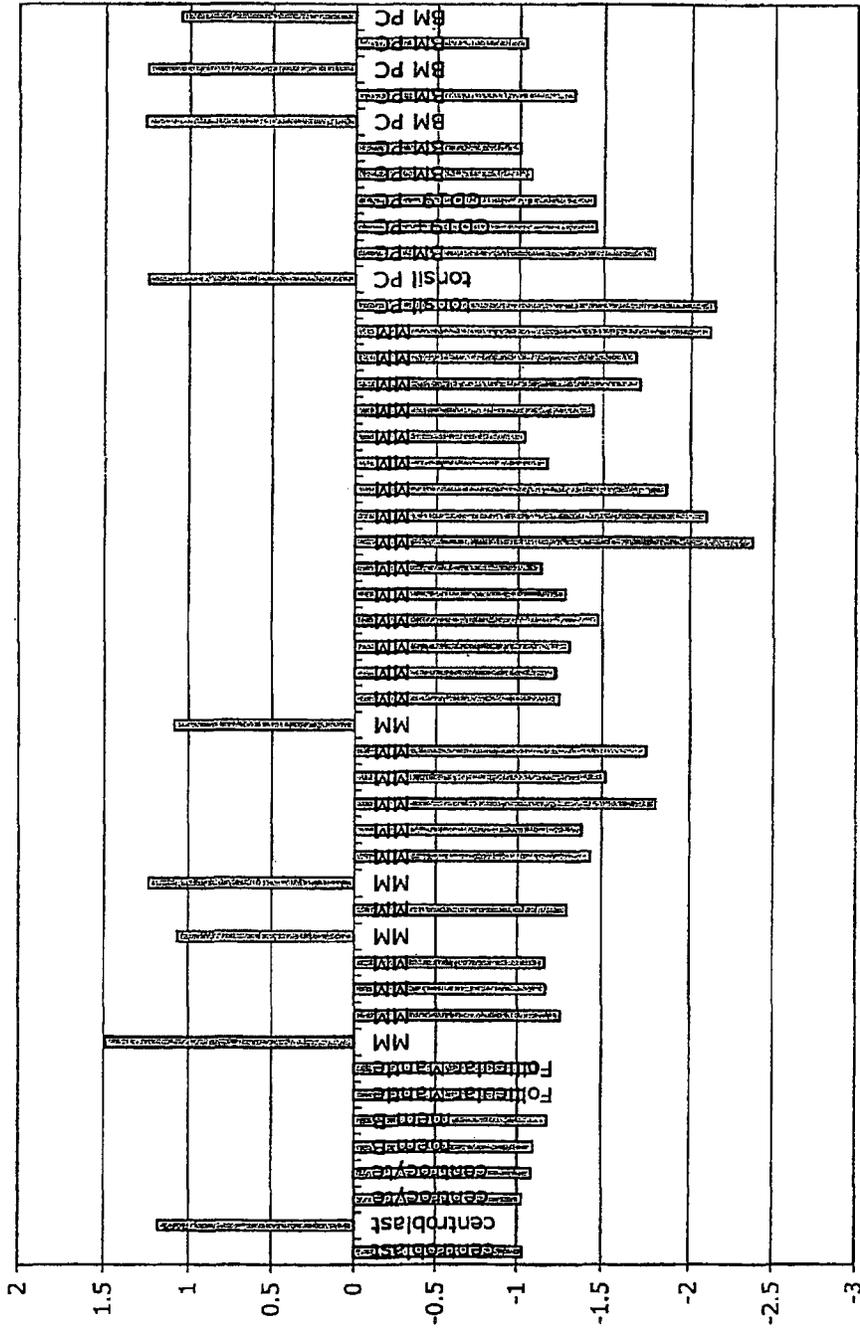
CR2



samples
FIGURE78B

TAH06/DNA225875/CD21 (CR2)

CR2



sample
FIGURE 78D

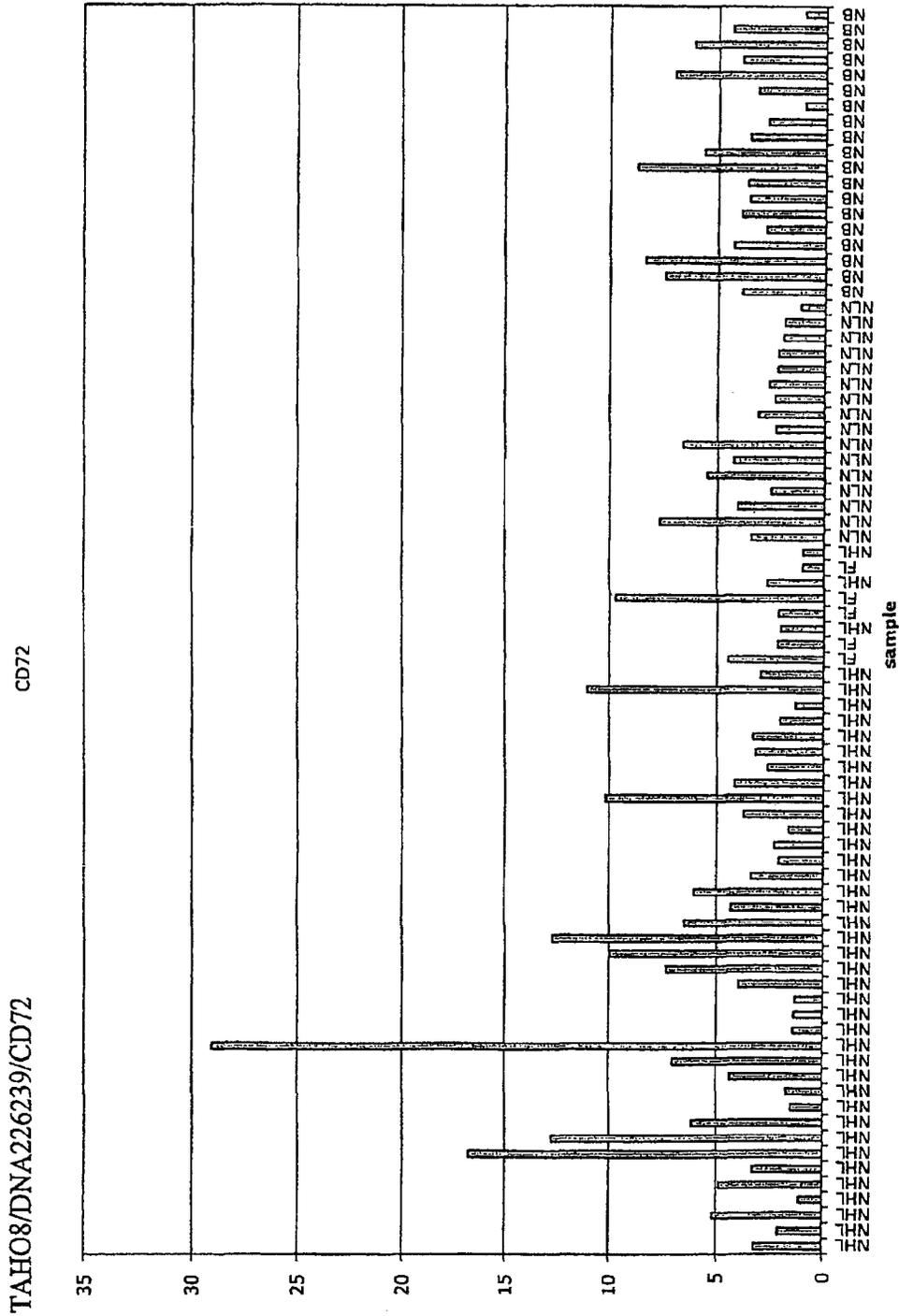
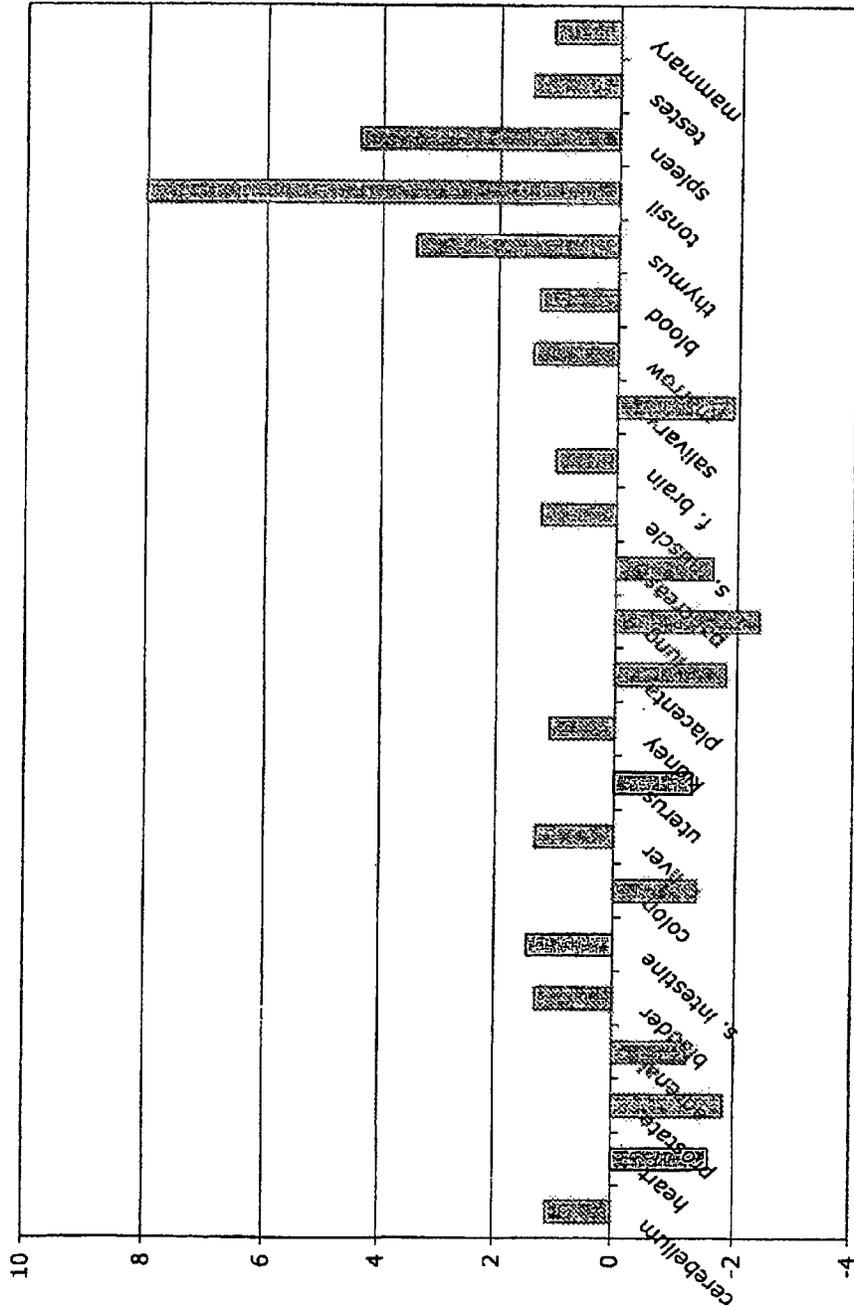


FIGURE 79A

TAHO8/DNA226239/CD72

CD72

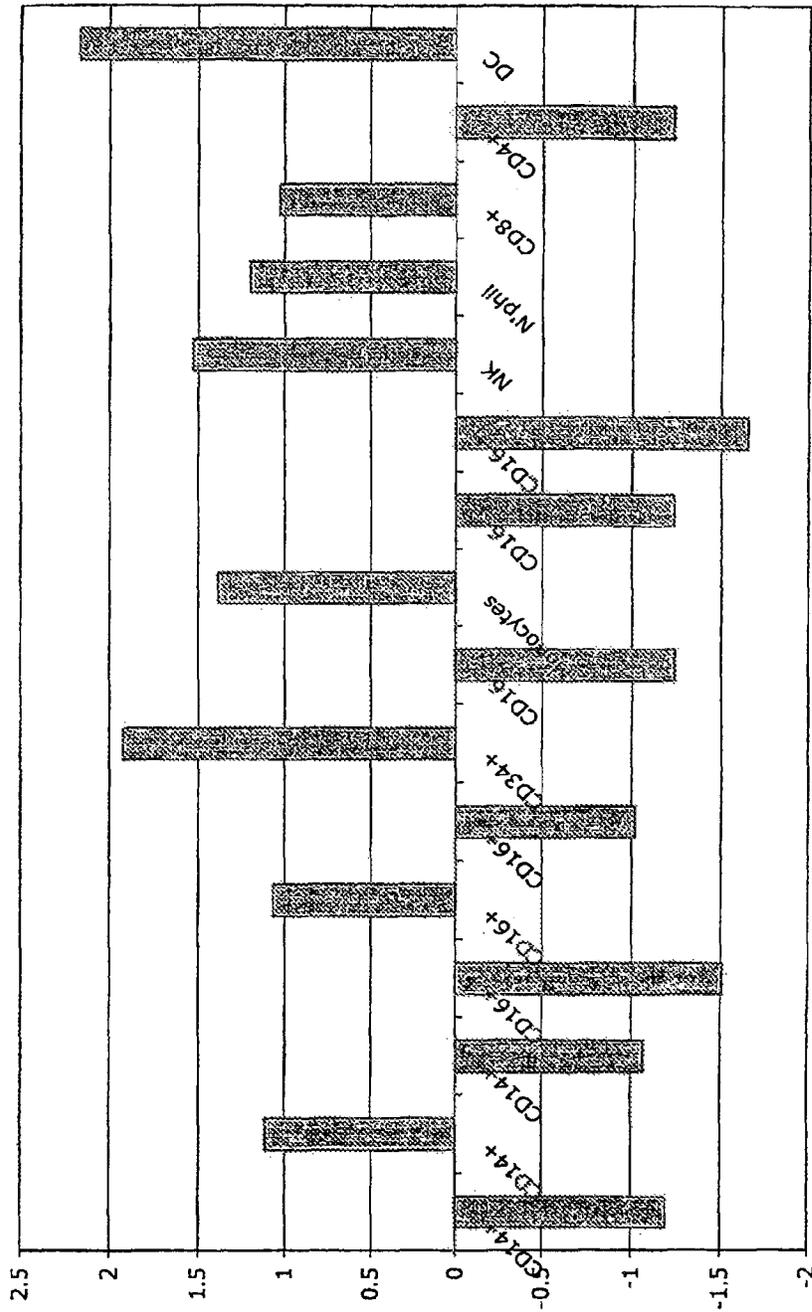


samples

FIGURE 79B

CD72

TAHO8/DNA226239/CD72



sample
FIGURE 79C

TAHO9/DNA226394/P2XR5
P2XR5 UNQ2170 purinergic receptor P2X, ligand-gated ion channel, 5

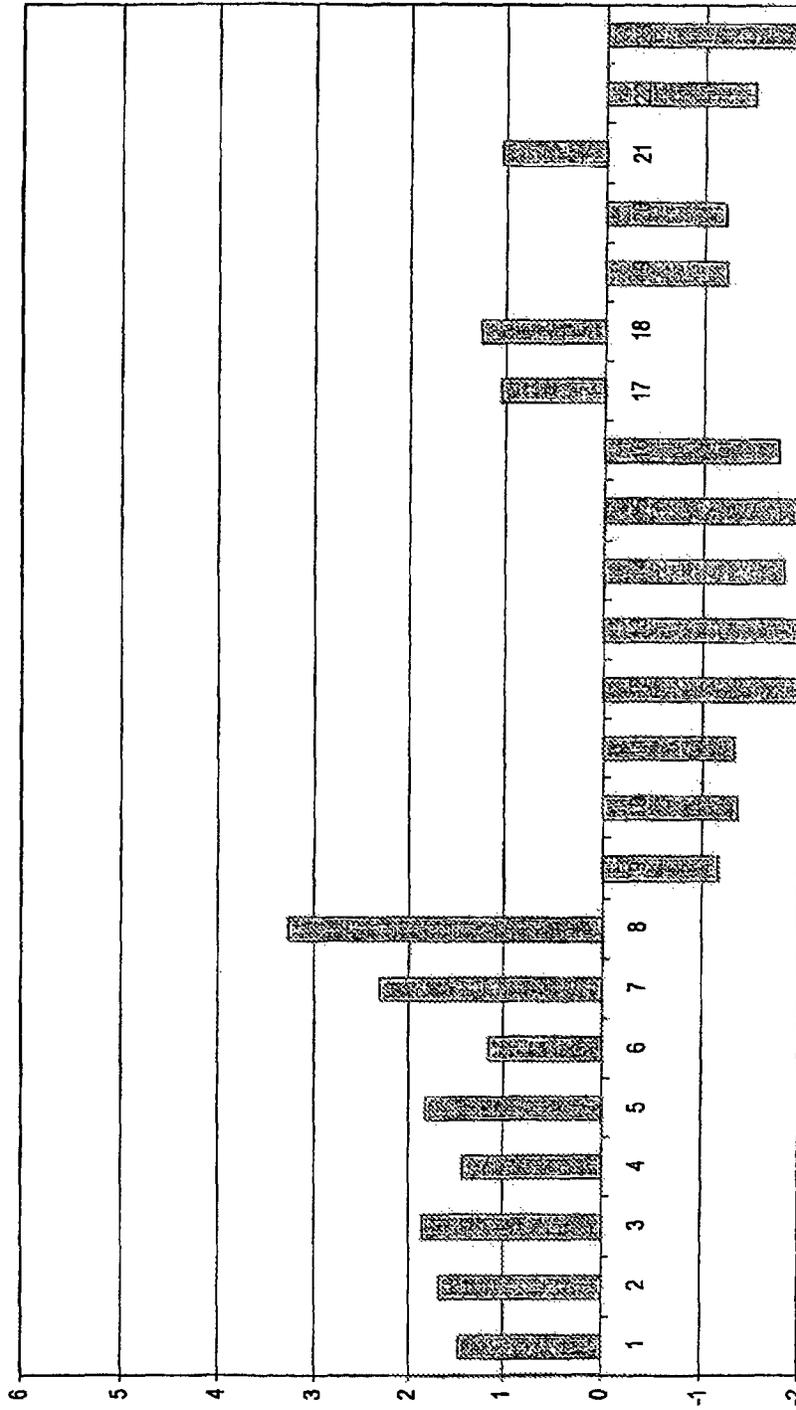


FIGURE 80A

TAHO9/DNA226394/P2XR5

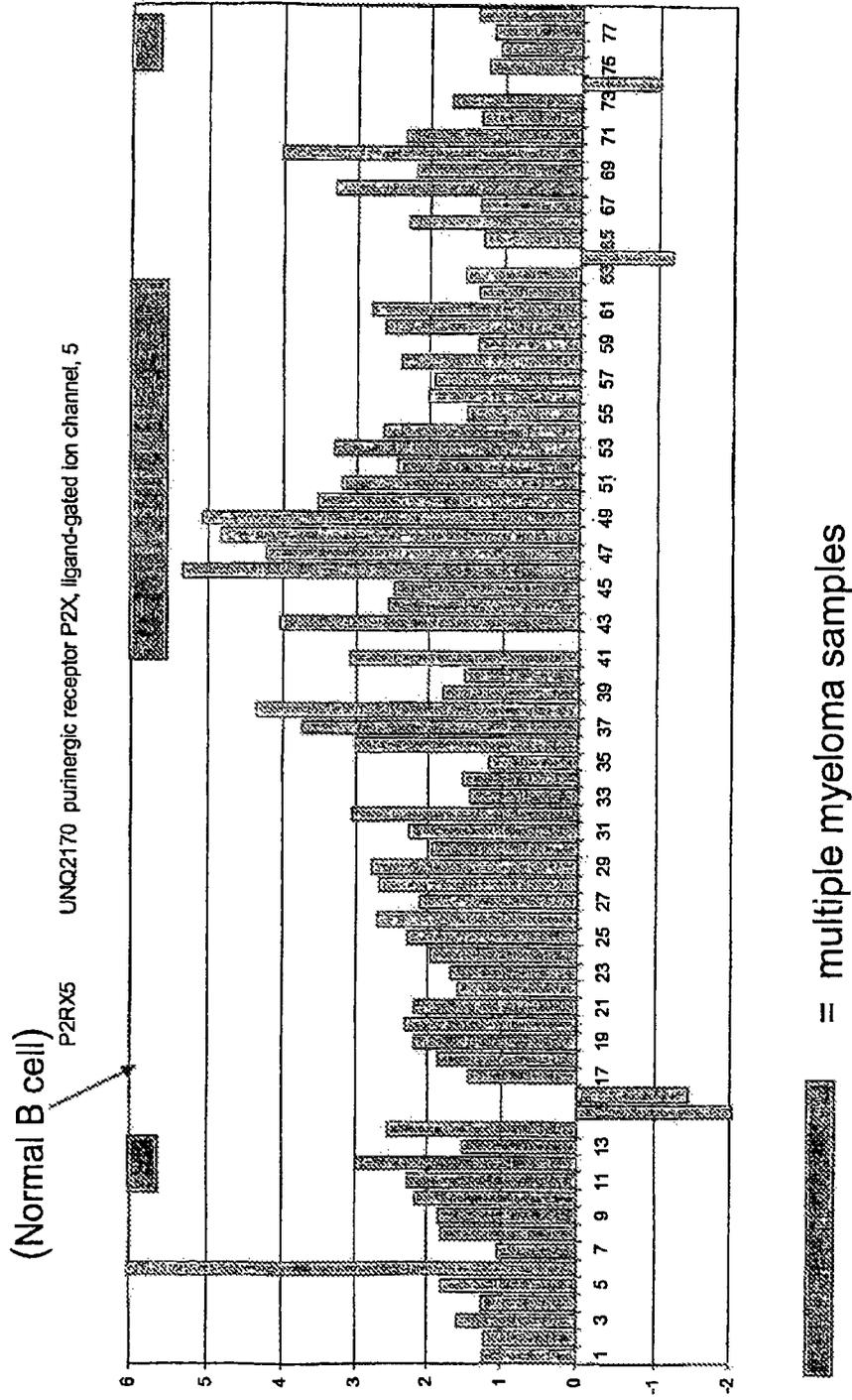
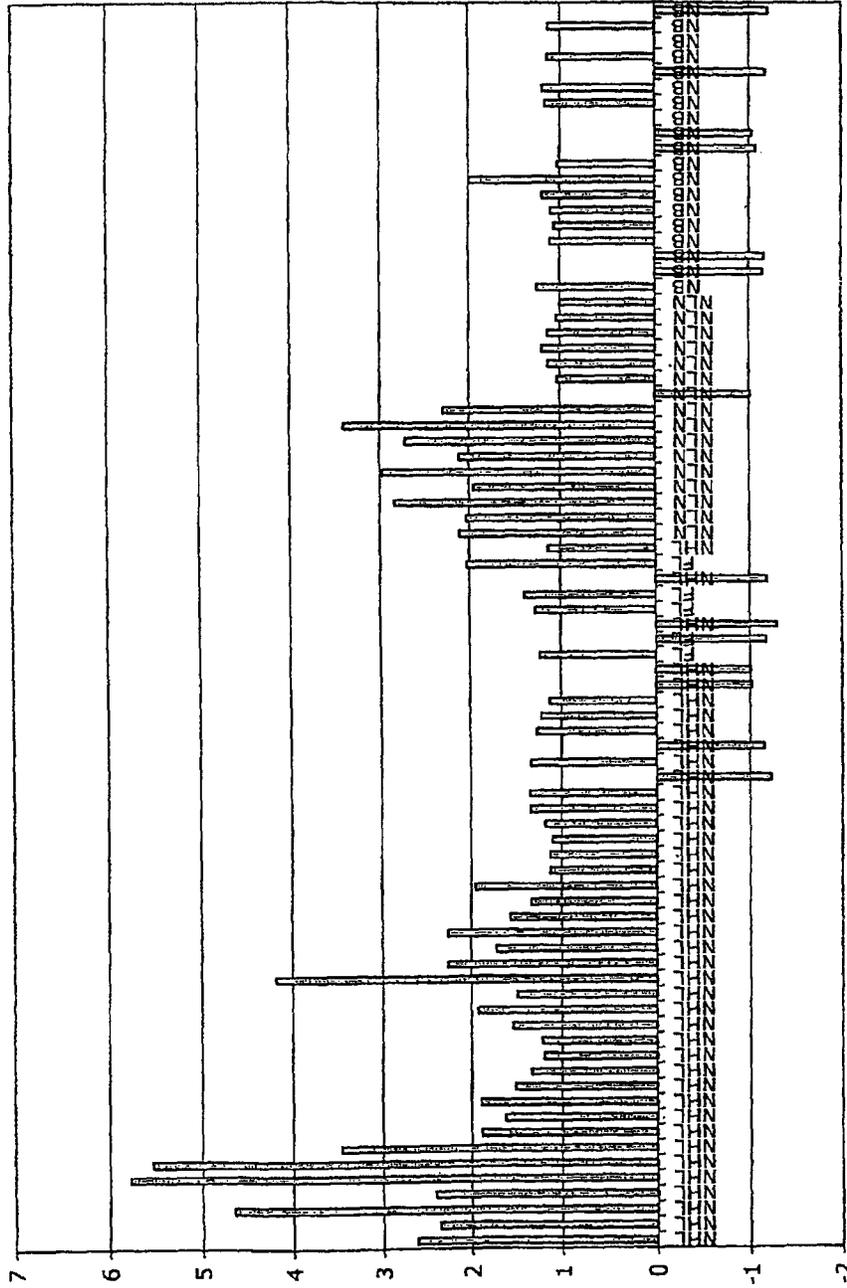


FIGURE 80B

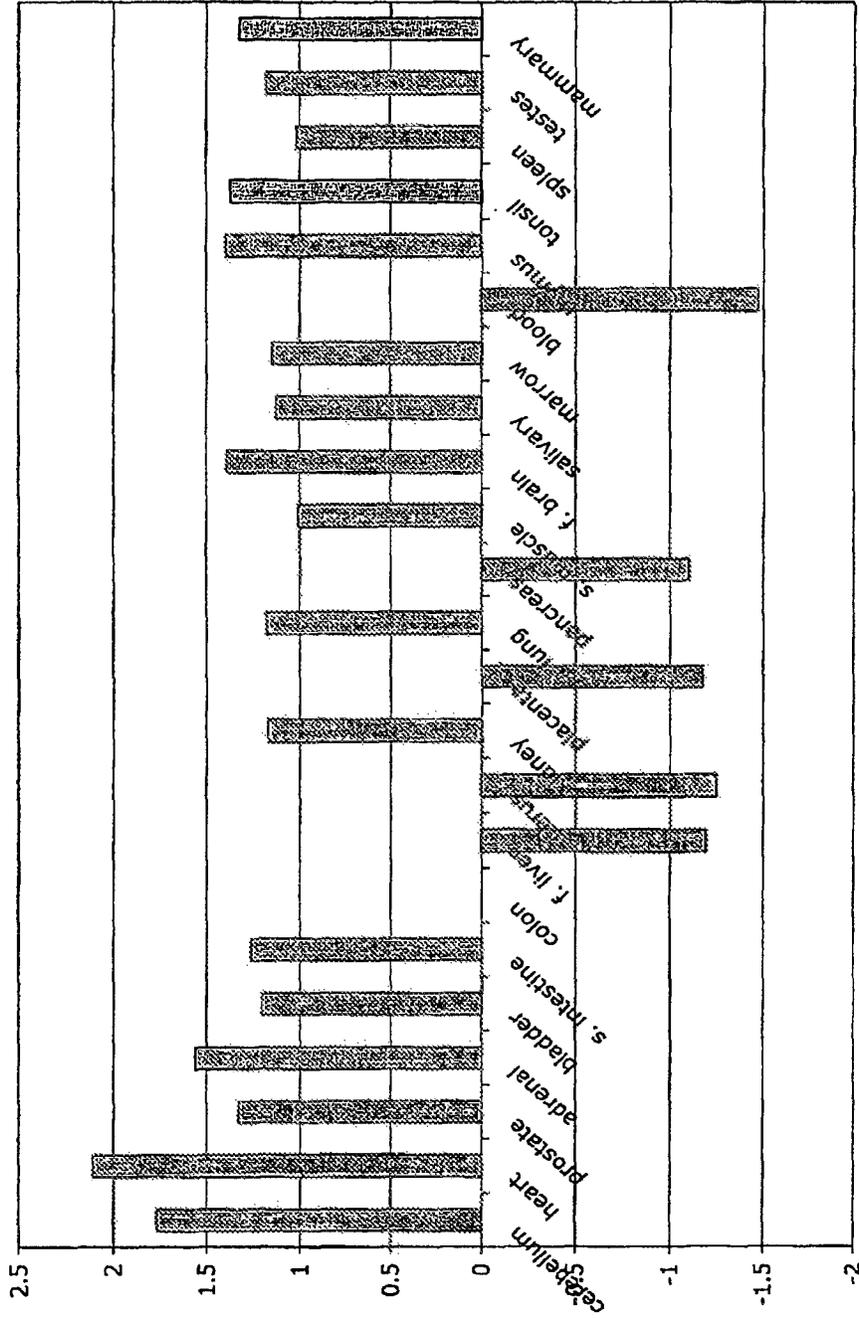
TAHO10/DNA226423/HLA-DOB

HLA-DOB



sample
FIGURE 81A

TAHO10/DNA226423/HLA-DOB HLA-DOB



samples
FIGURE 81B

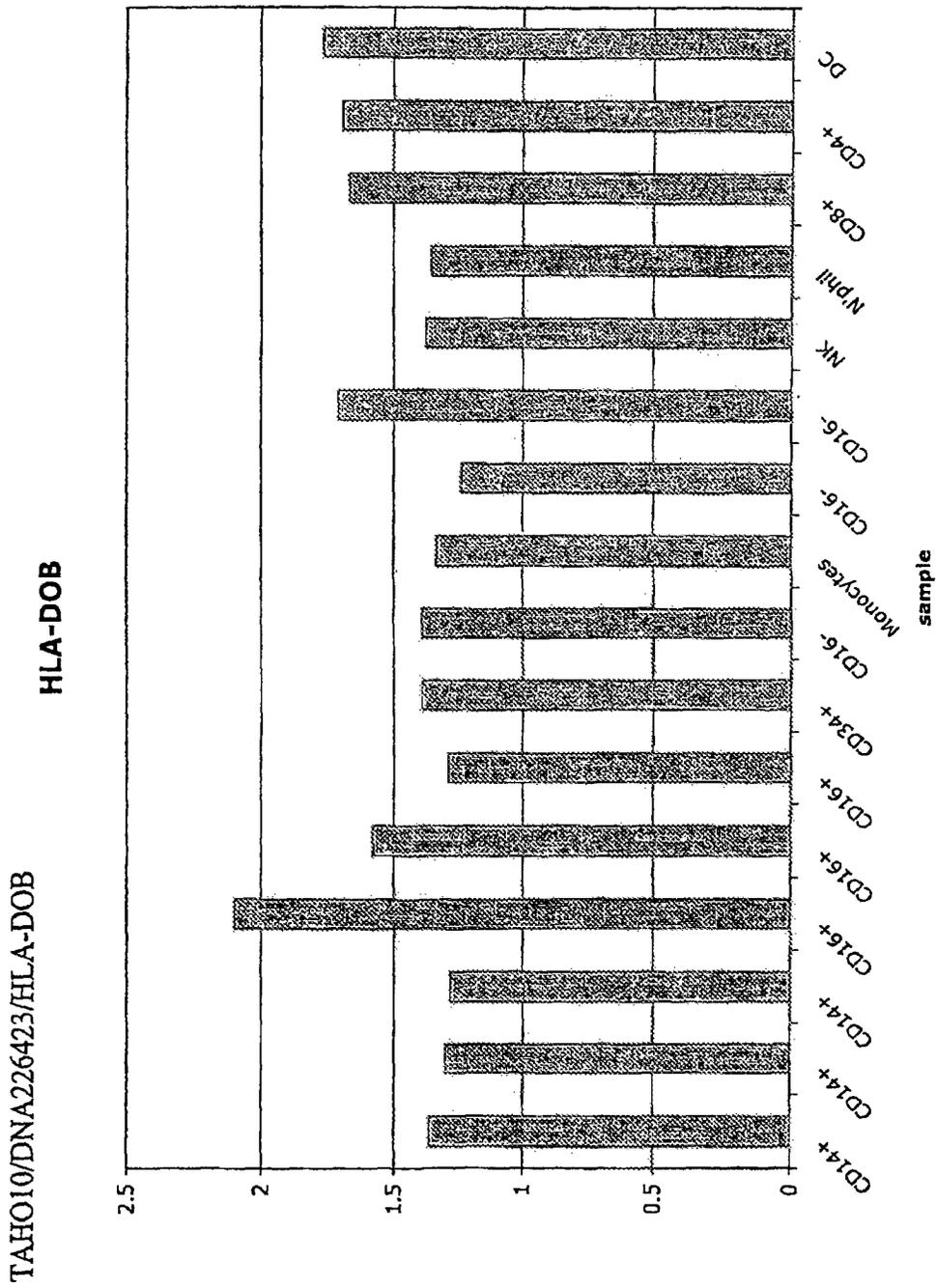
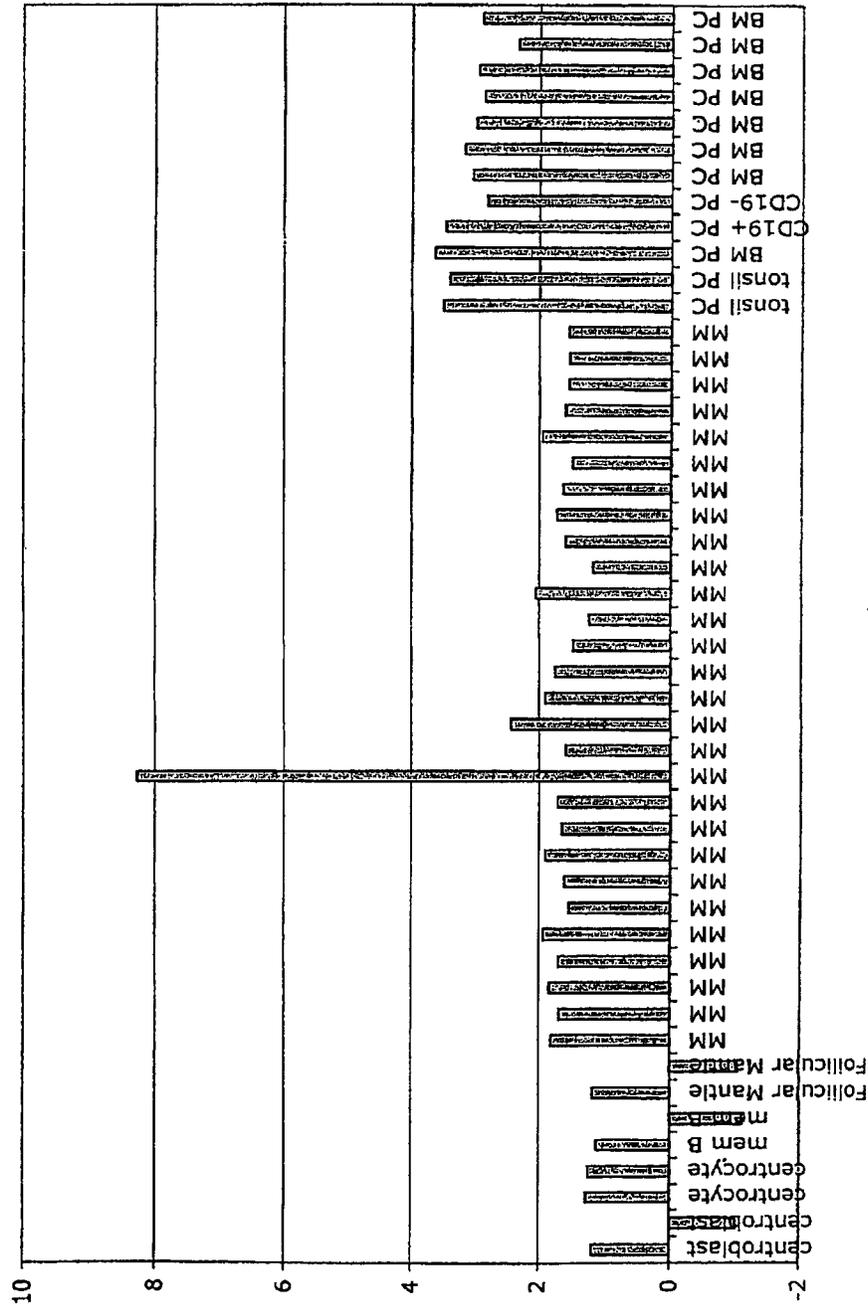


FIGURE 81C

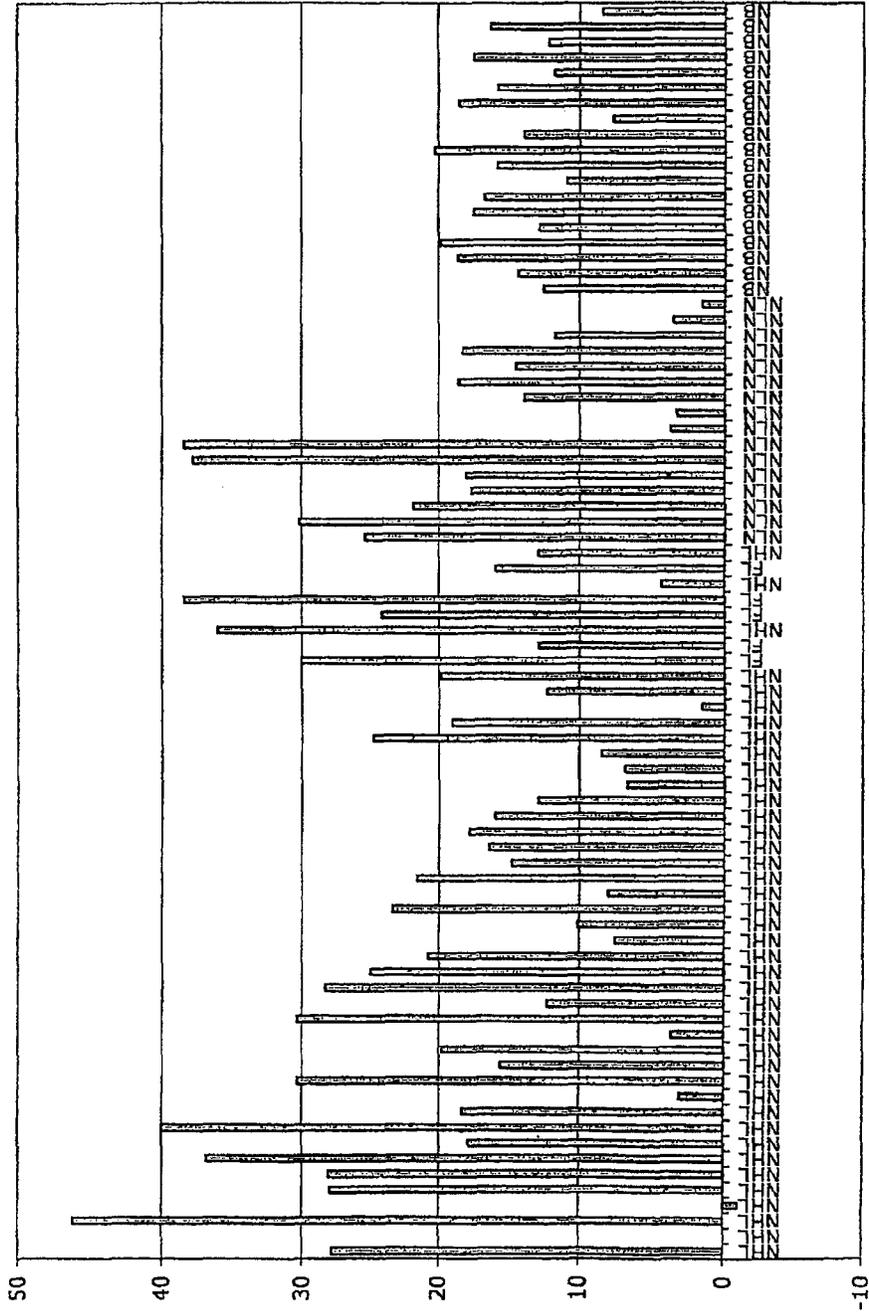
TAHO10/DNA226423/HLA-DOB

HLA-DOB



TAHO11/DNA227781/CXCR5 (BLR1)

BLR1



sample
FIGURE 82A

BLR1

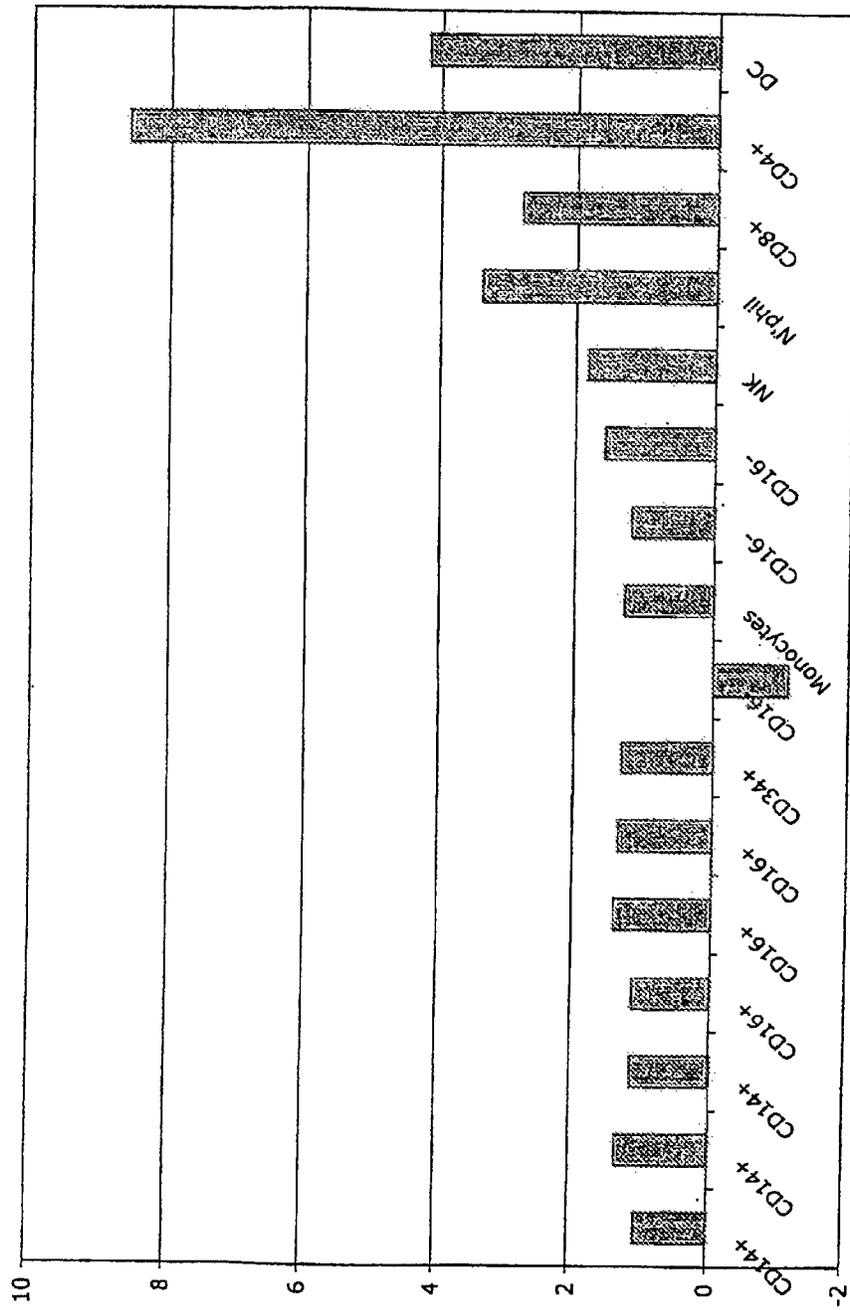
TAHO11/DNA227781/CXCR5 (BLR1)



samples
FIGURE 82B

TAHO11/DNA227781/CXCR5 (BLR1)

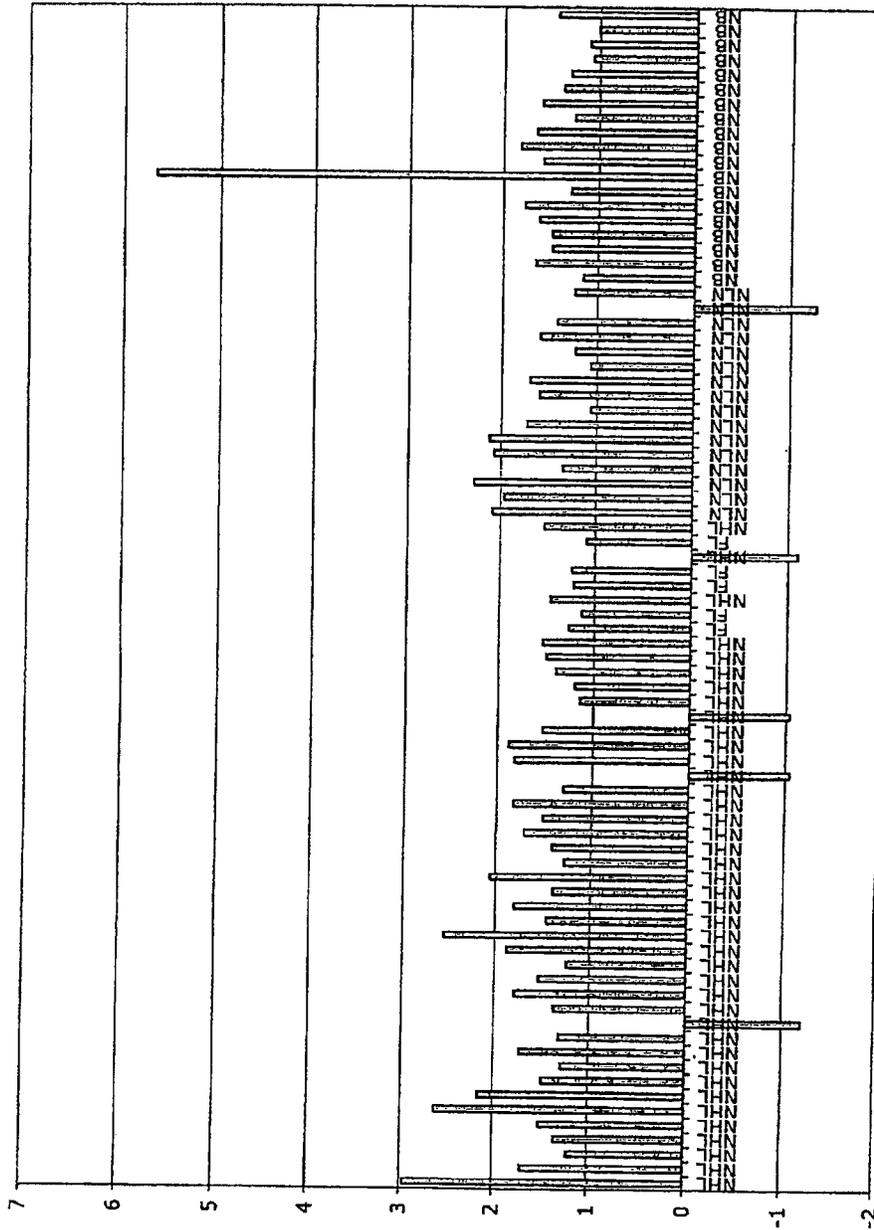
BLR1



sample
FIGURE 82C

TAHO12/DNA227879/FCER2

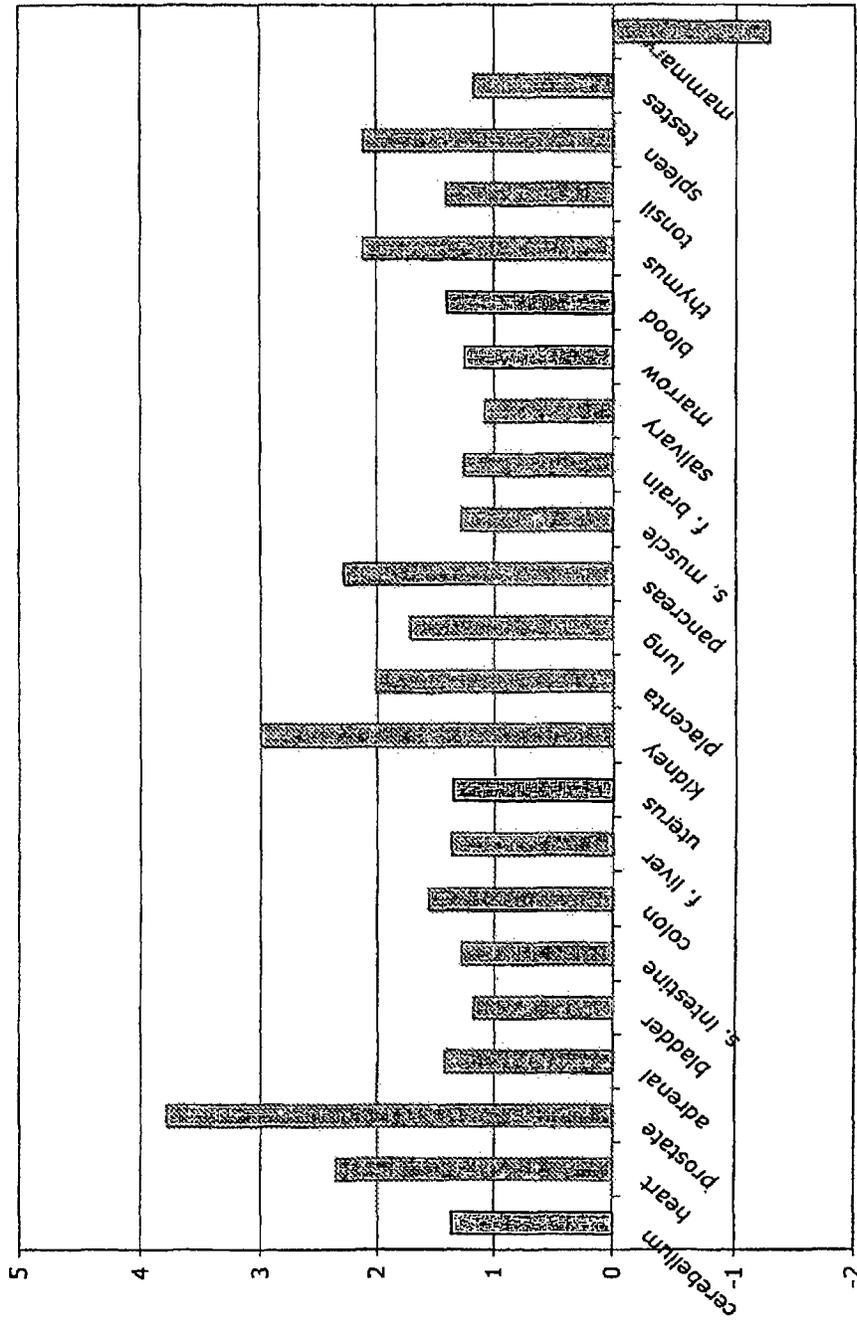
FCER2



sample
FIGURE 83A

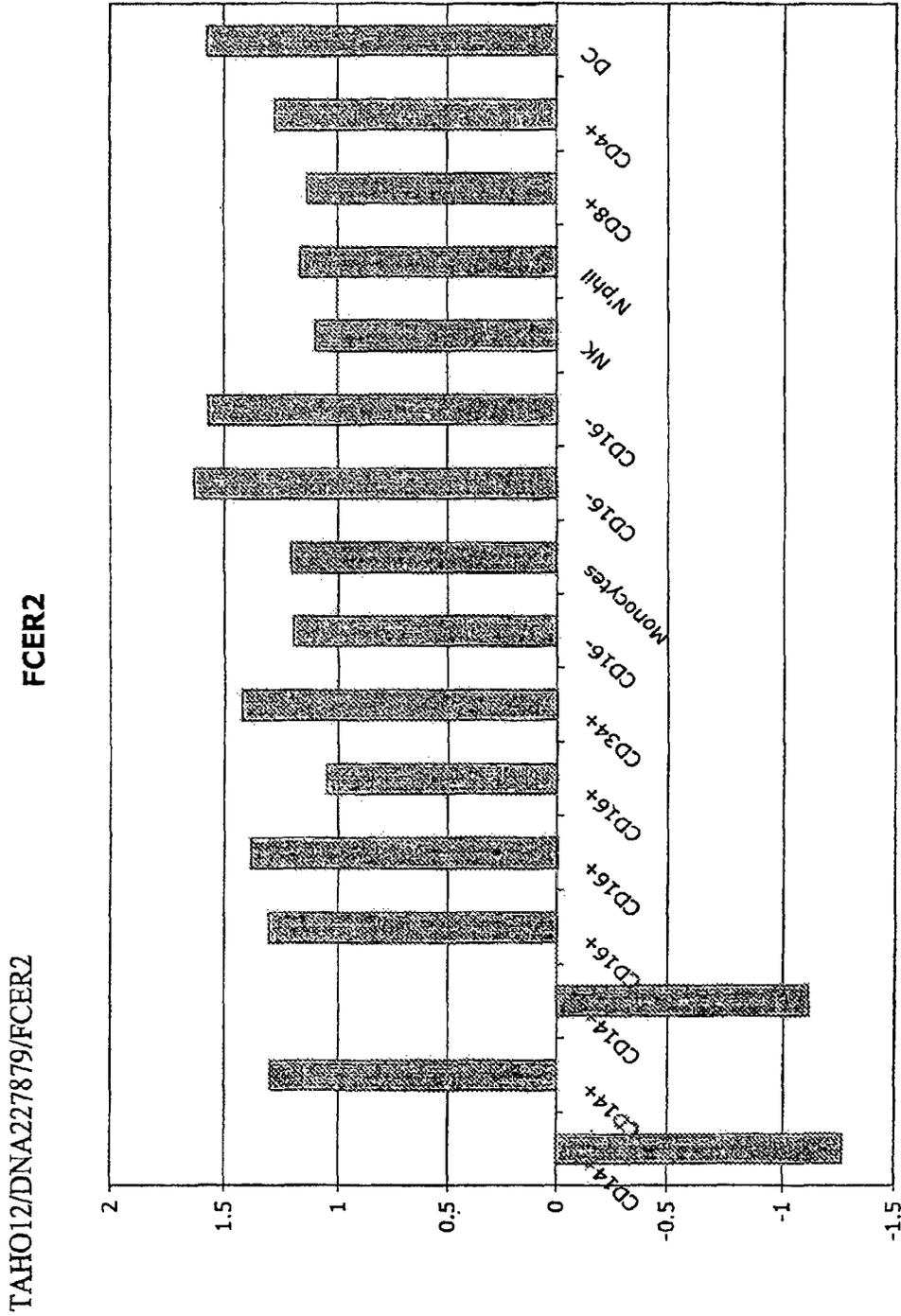
TAHO12/DNA227879/FCER2

FCER2



samples

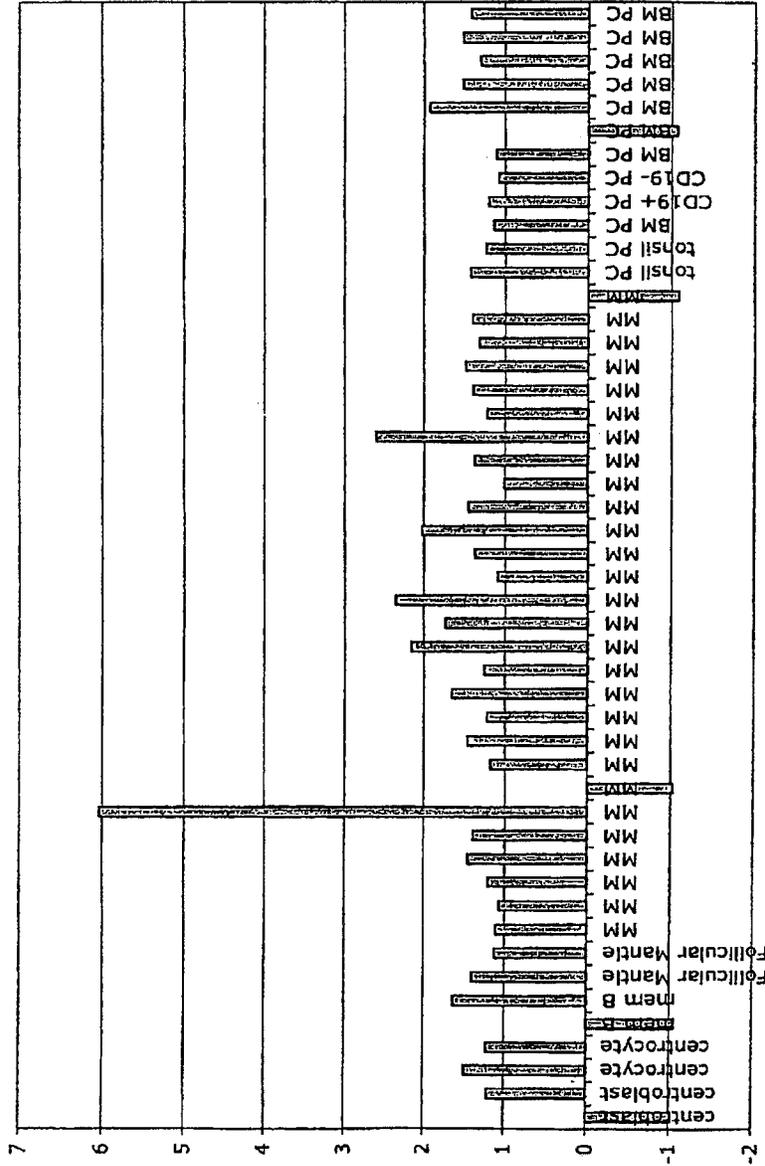
FIGURE 83B



sample
FIGURE 83C

TAHO12/DNA227879/FCER2

FCER2



sample

FIGURE 83D

TAHOI13/DNA256363/GPR2

GPR2 UNQ12100

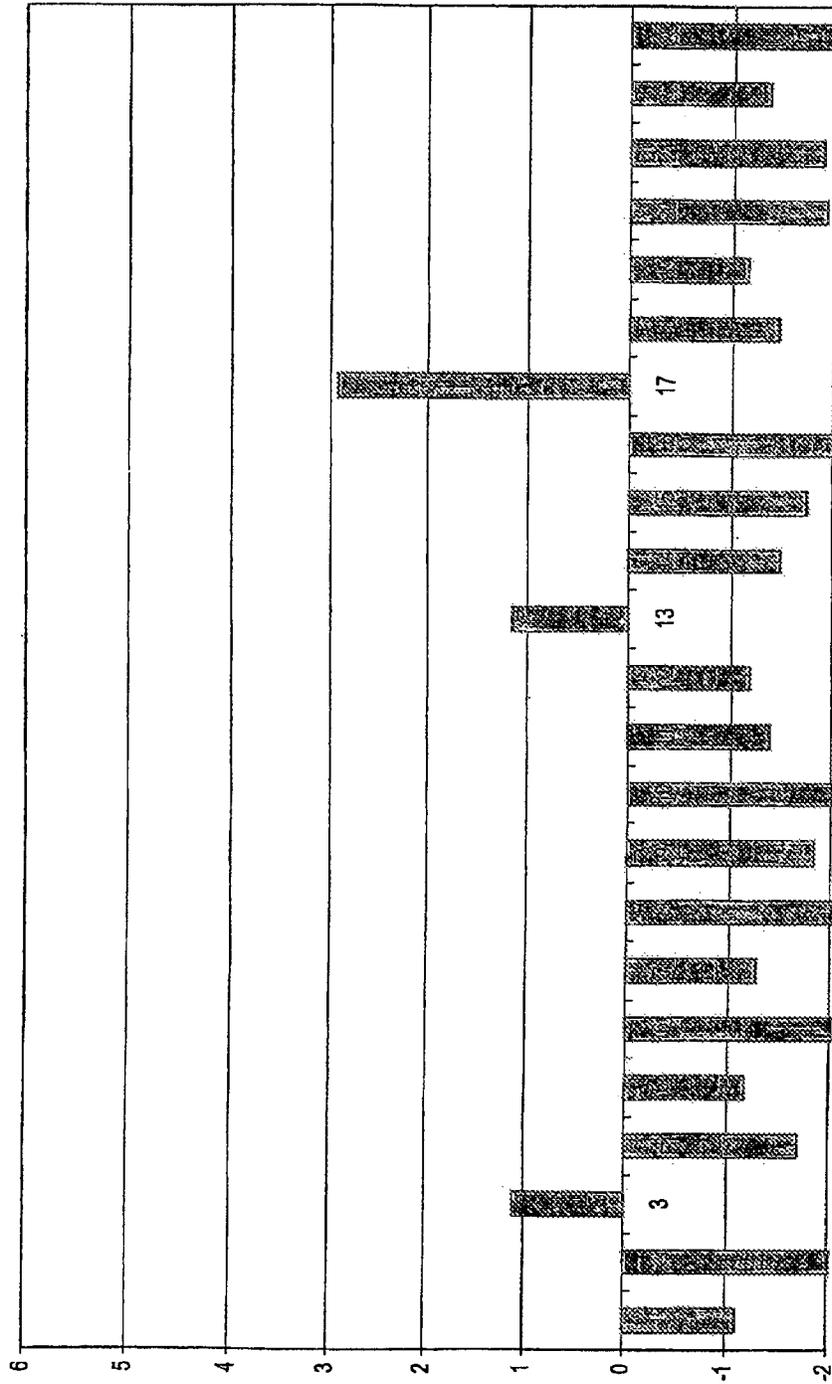
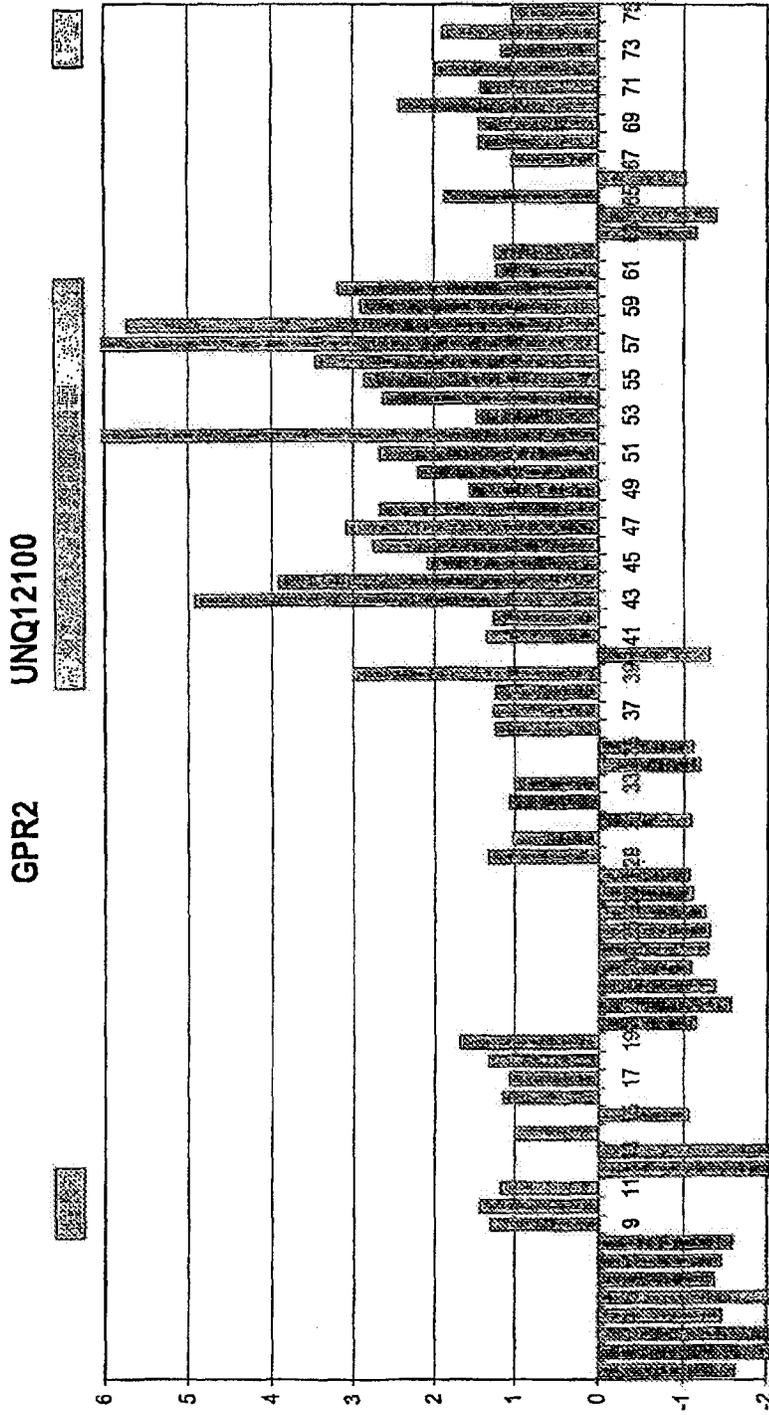


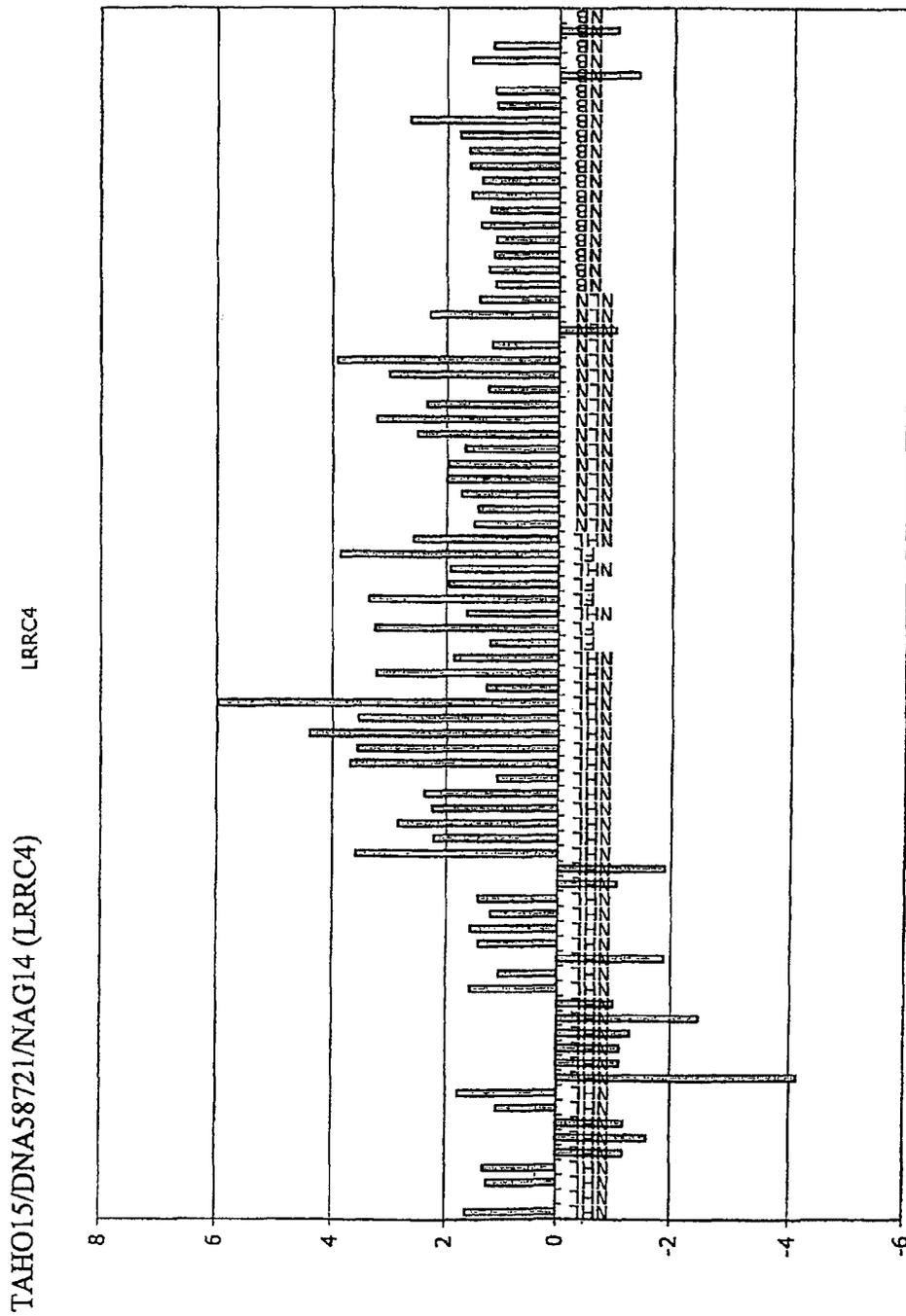
FIGURE 84A

TAHO13/DNA256363/GPR2

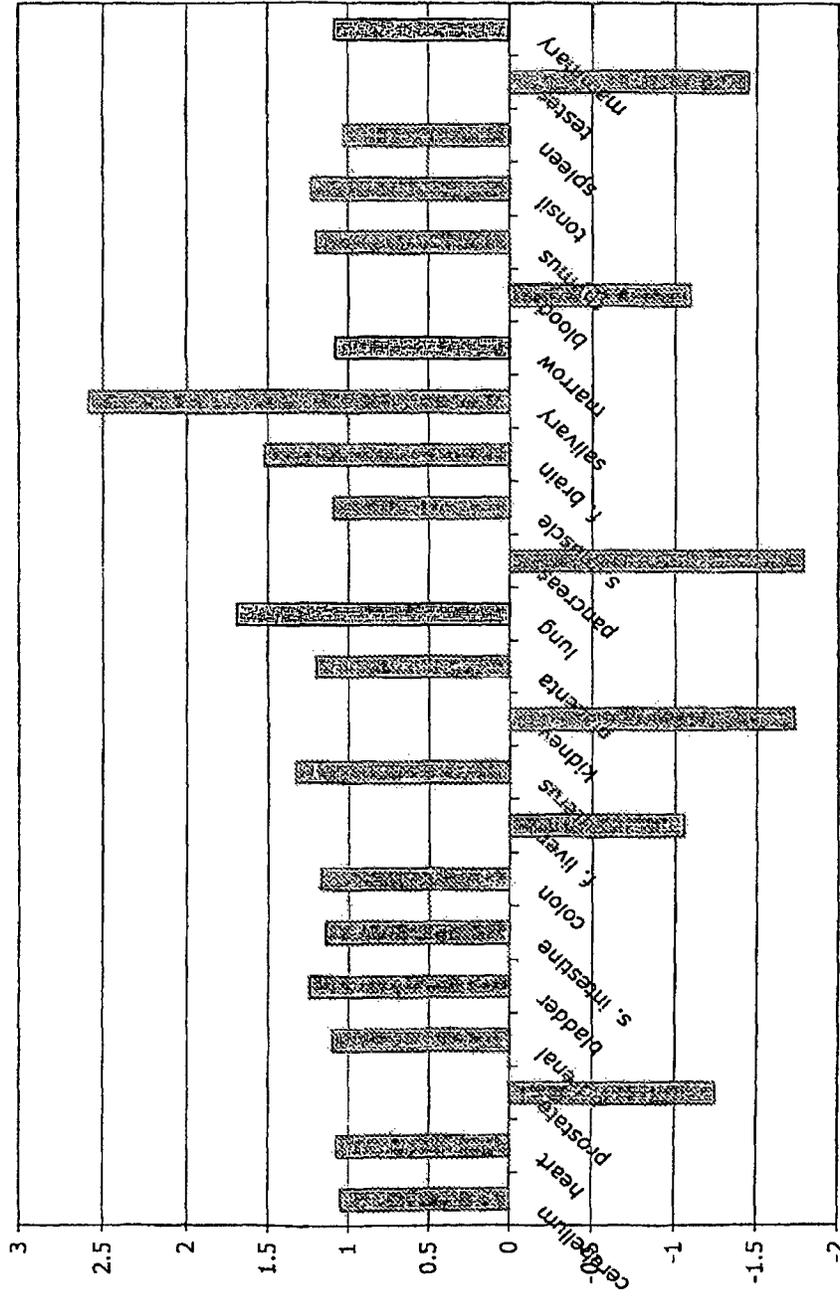


= multiple myeloma samples

FIGURE 84B



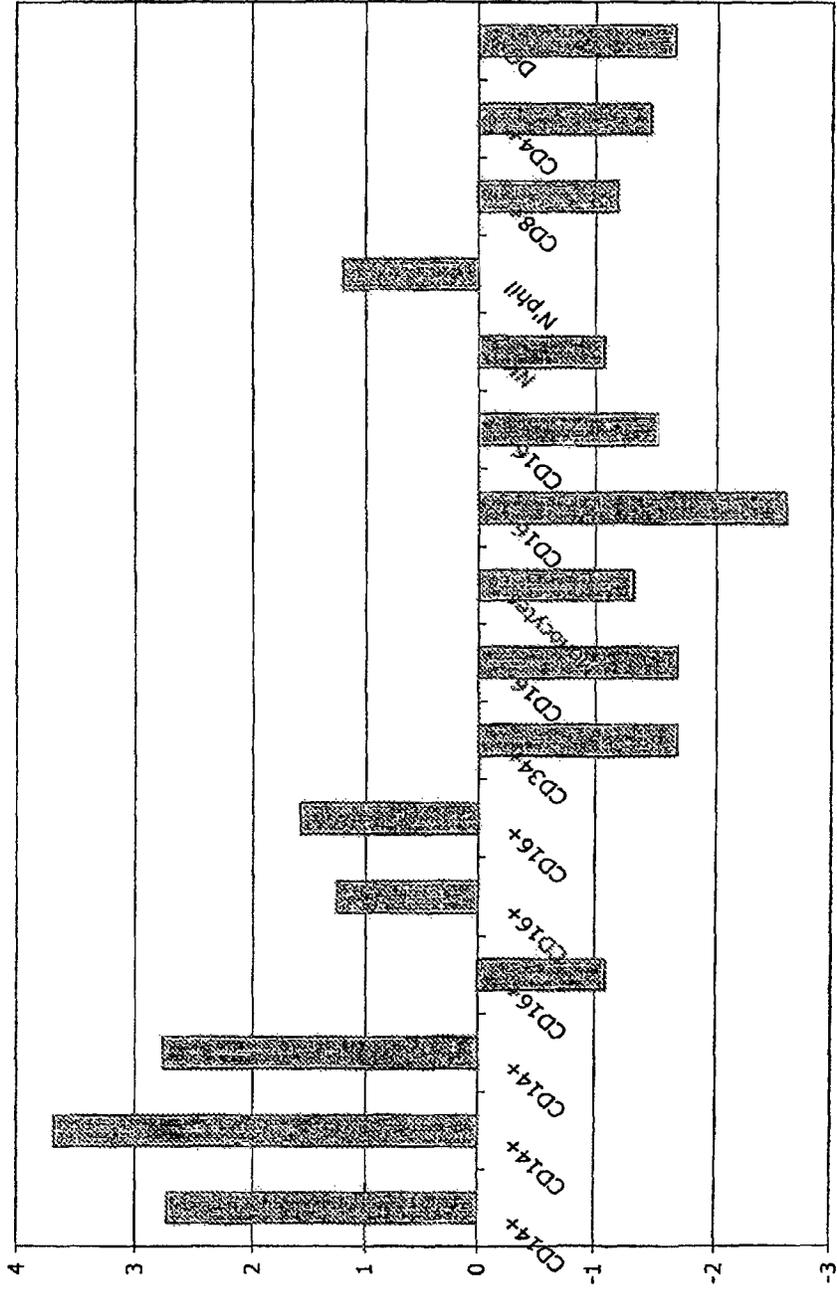
TAHO15/DNA58721/NAG14 (LRRRC4)



samples
FIGURE 85B

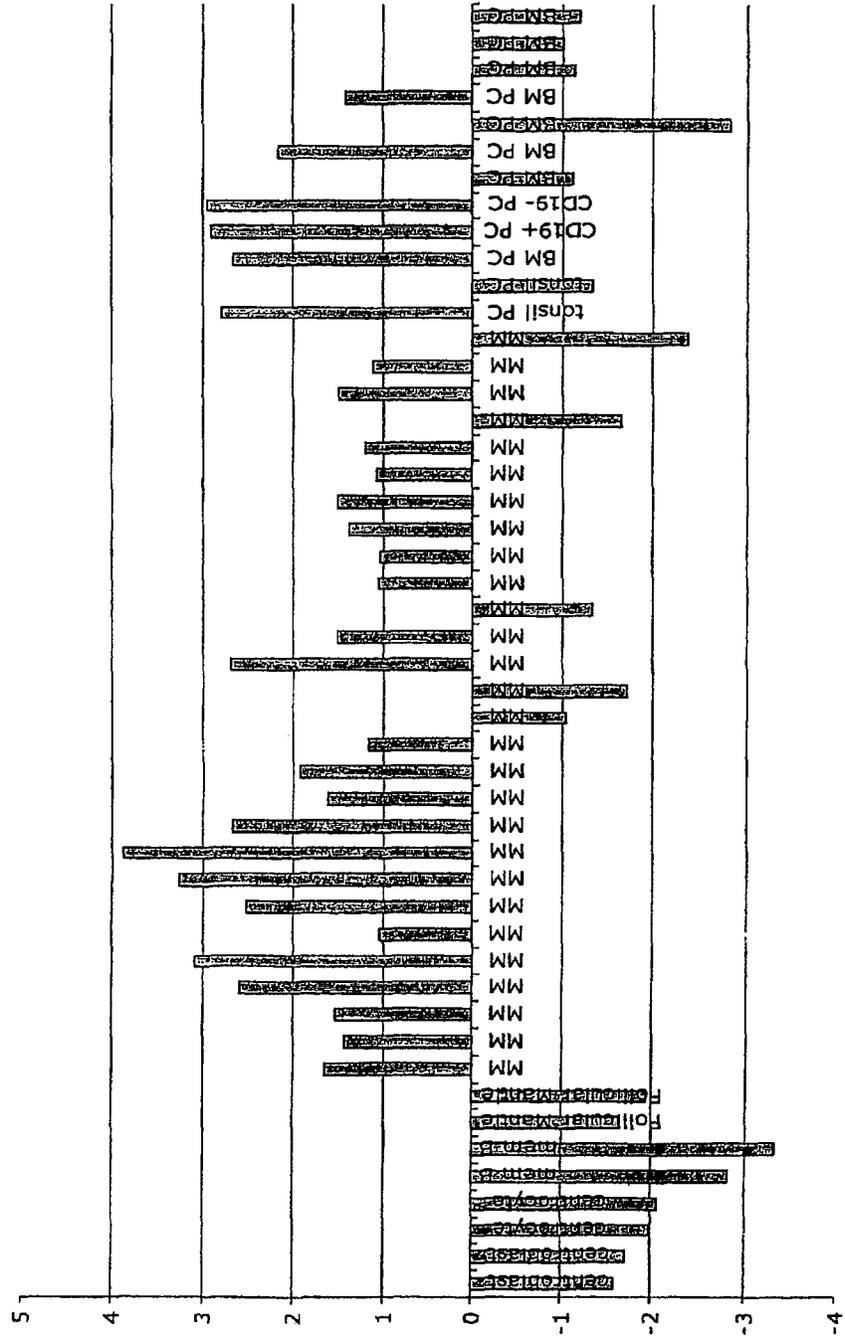
TAHO15/DNA58721/NAG14 (LRRC4)

LRRC4



sample
FIGURE 85C

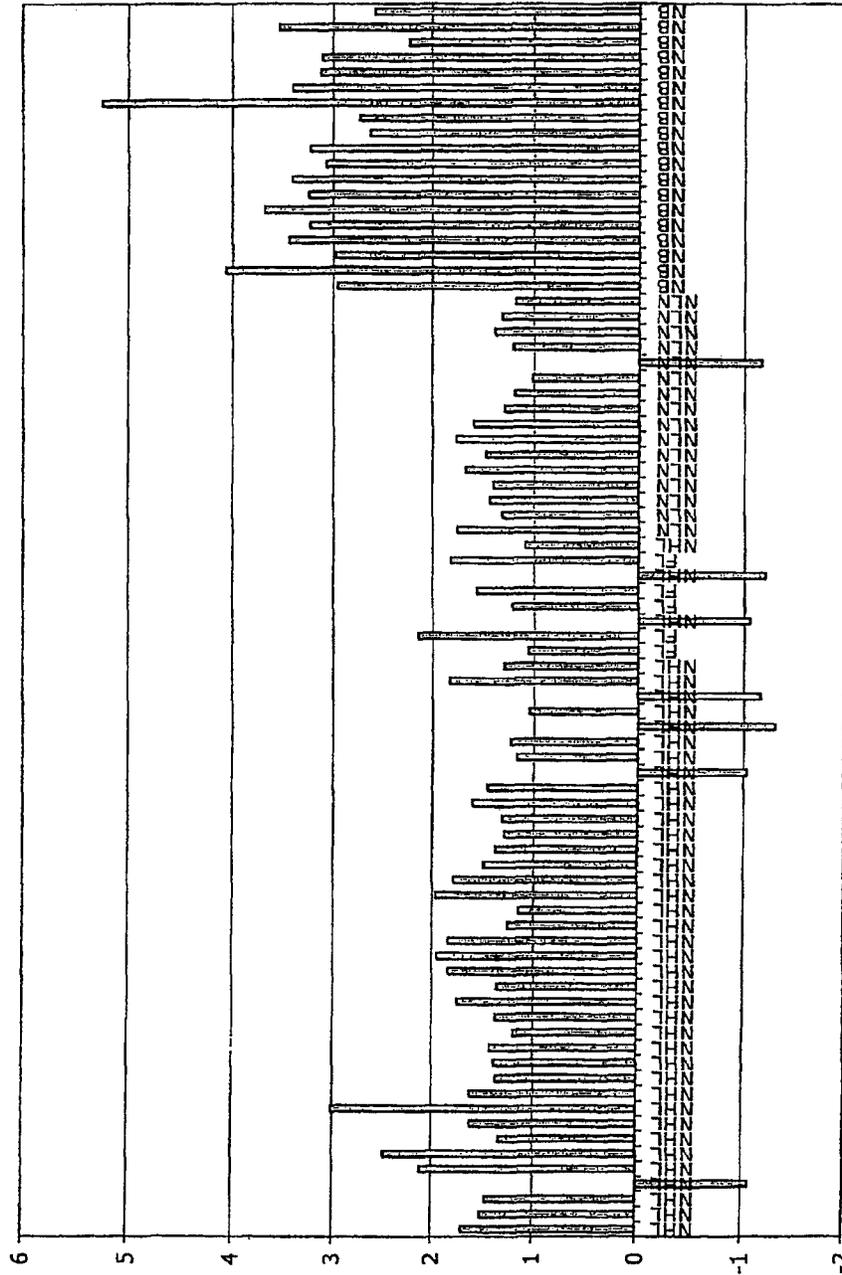
TAHO15/DNA58721/NAG14 (LRRC4) LRRC4



sample FIGURE 85D

TAHO17/DNA340394/FcRH1

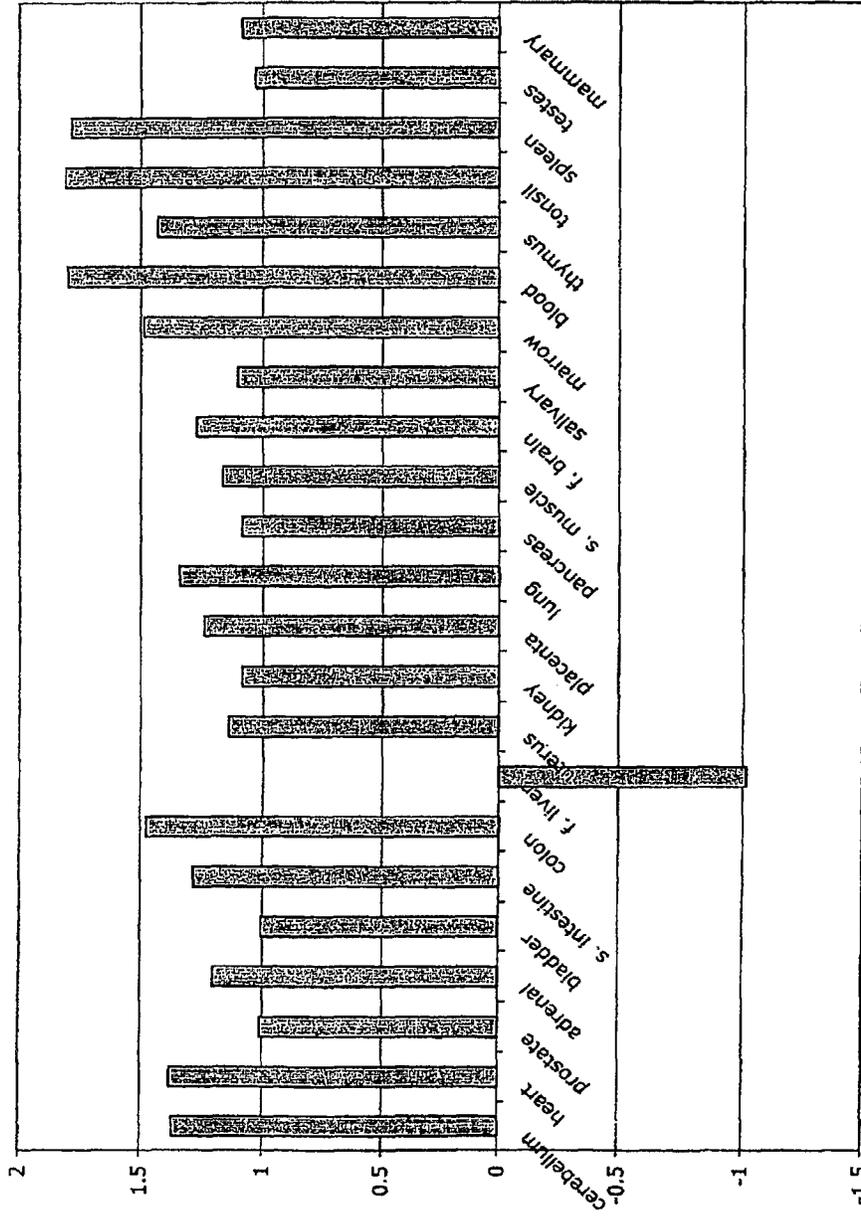
FcRH1



sample
FIGURE 86A

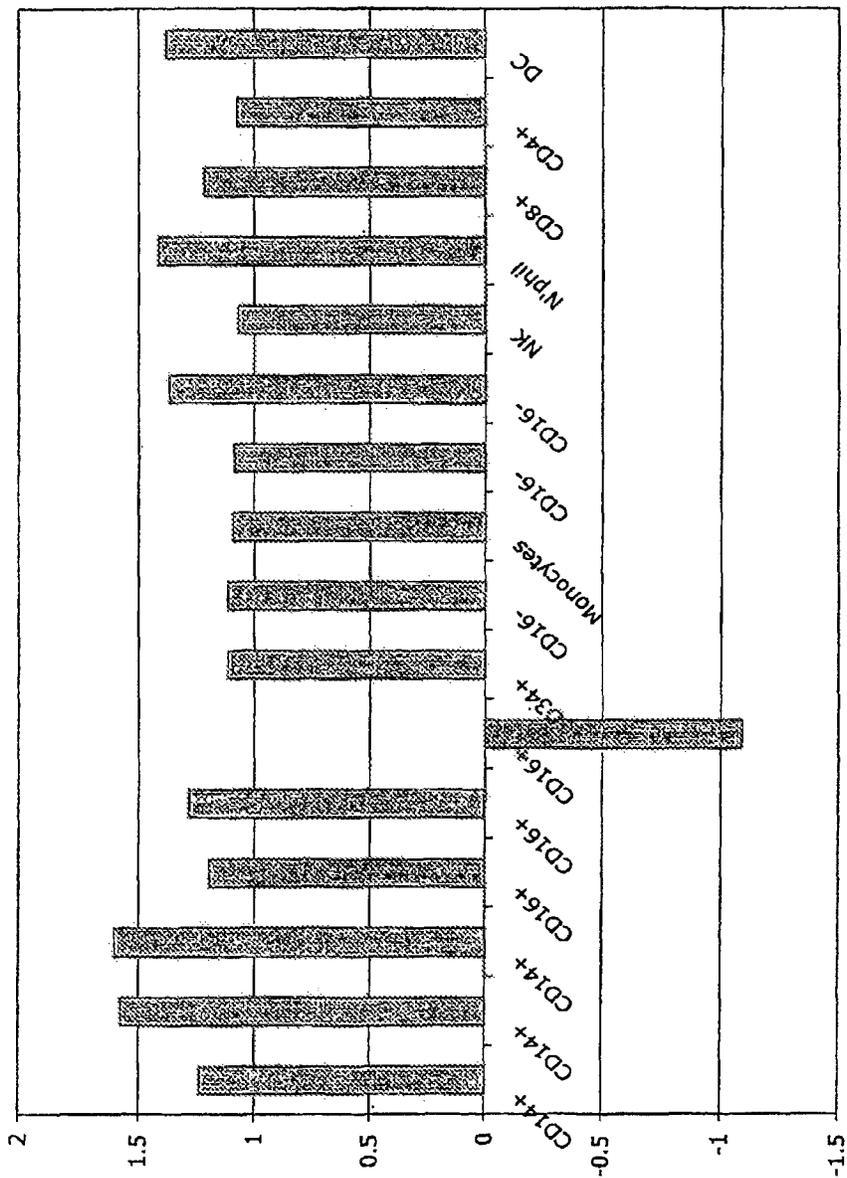
TAHO17/DNA340394/FcRH1

FCRH1



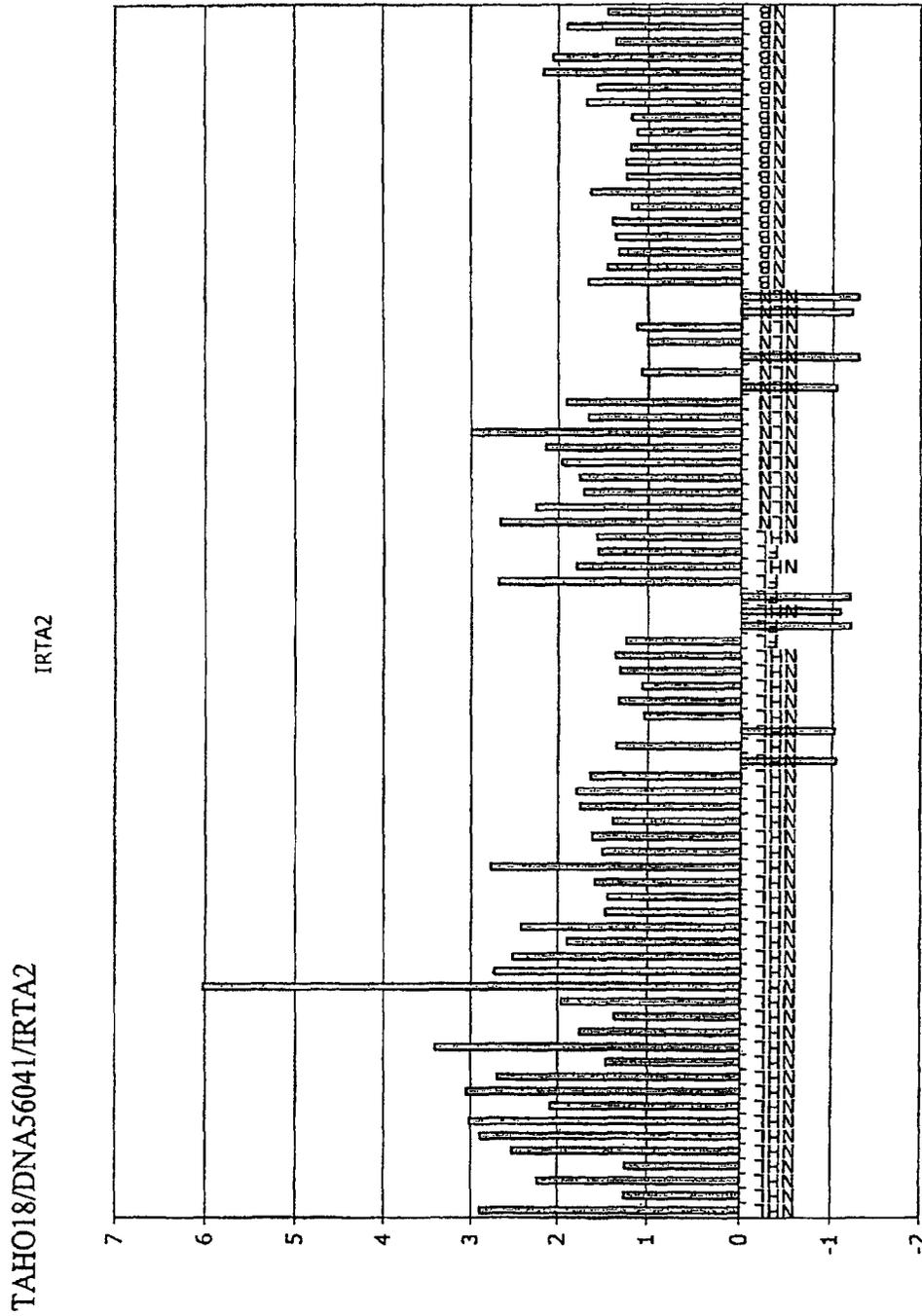
samples
FIGURE 86B

TAHO17/DNA340394/FcRH1 FCRH1



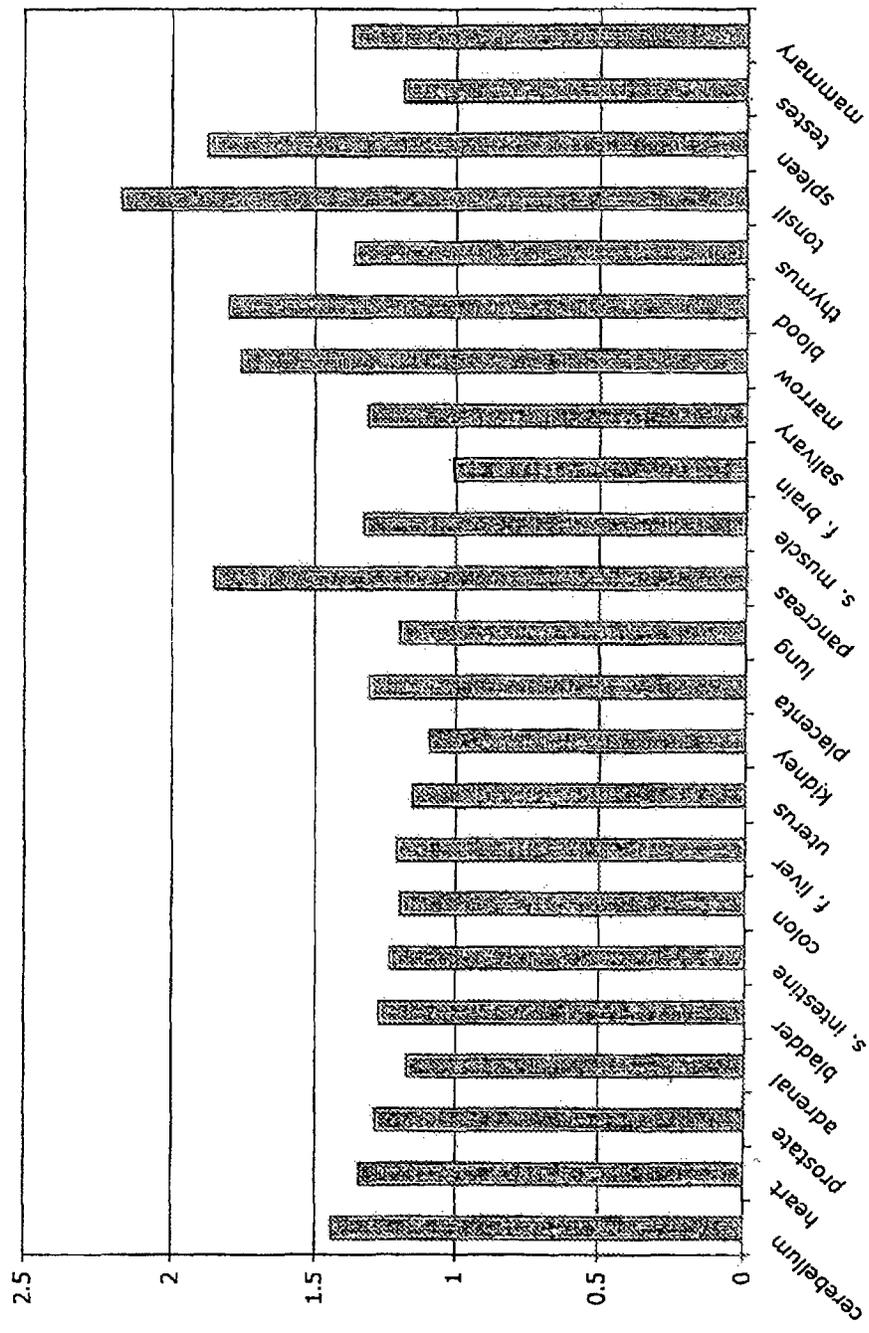
sample

FIGURE 86C



TAHO18/DNA56041/IRTA2

IRTA2



samples
FIGURE 87B

TAHO18/DNA56041/IRTA2

IRTA2

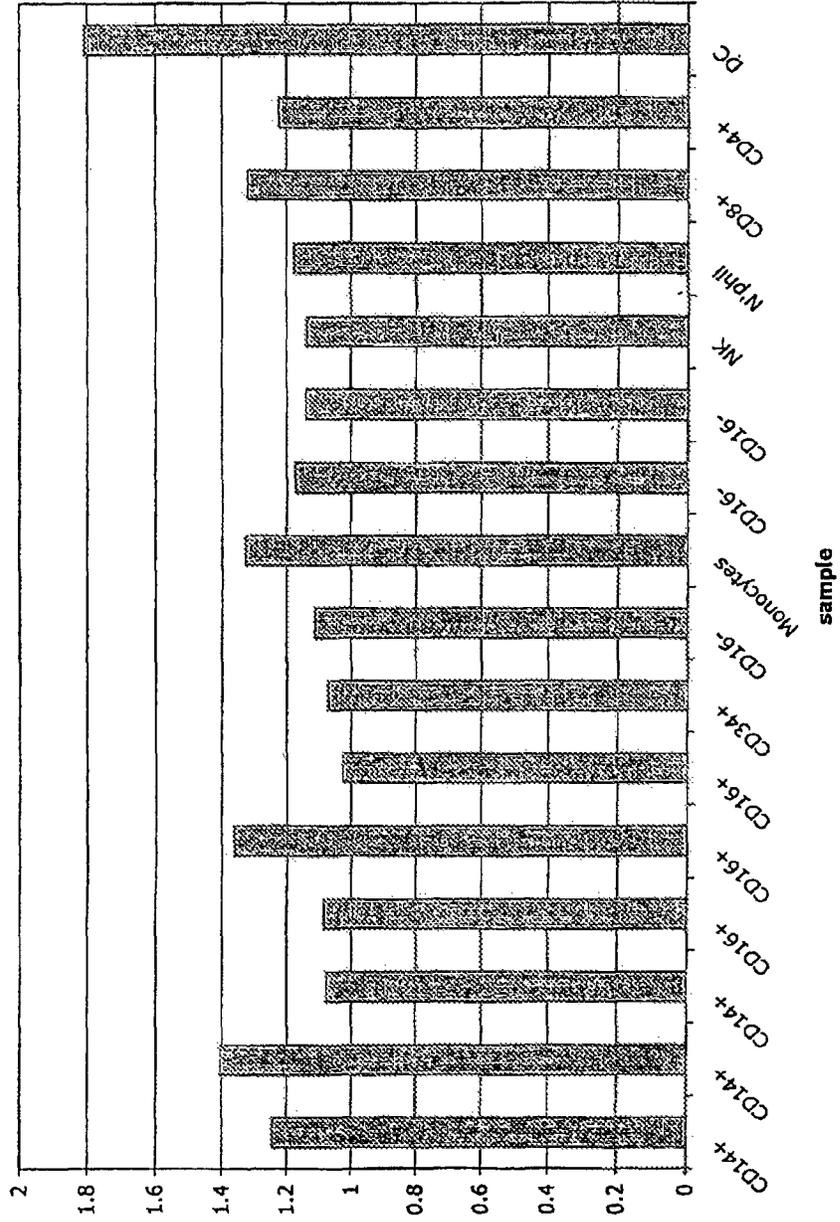
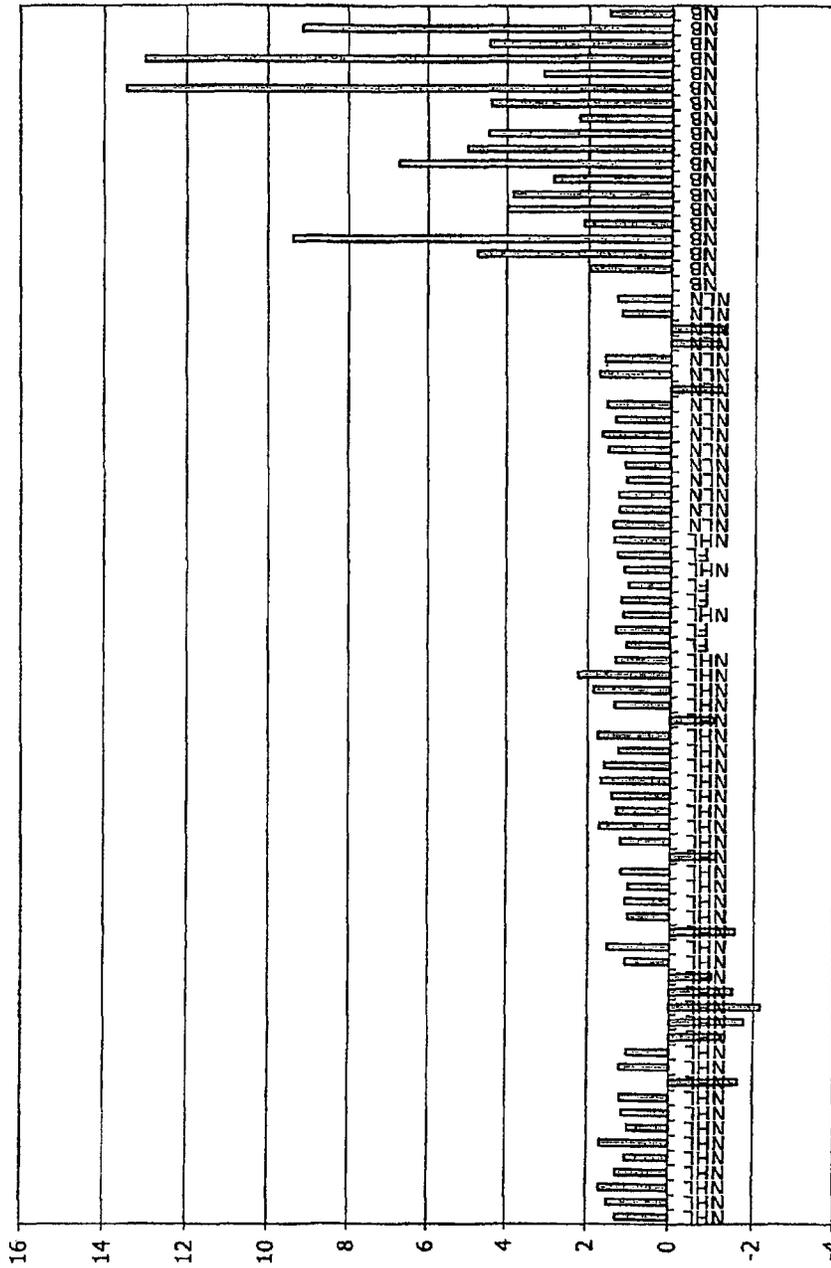


FIGURE 87C

TAHO20/DNA257955/FcRH3

FCRH3

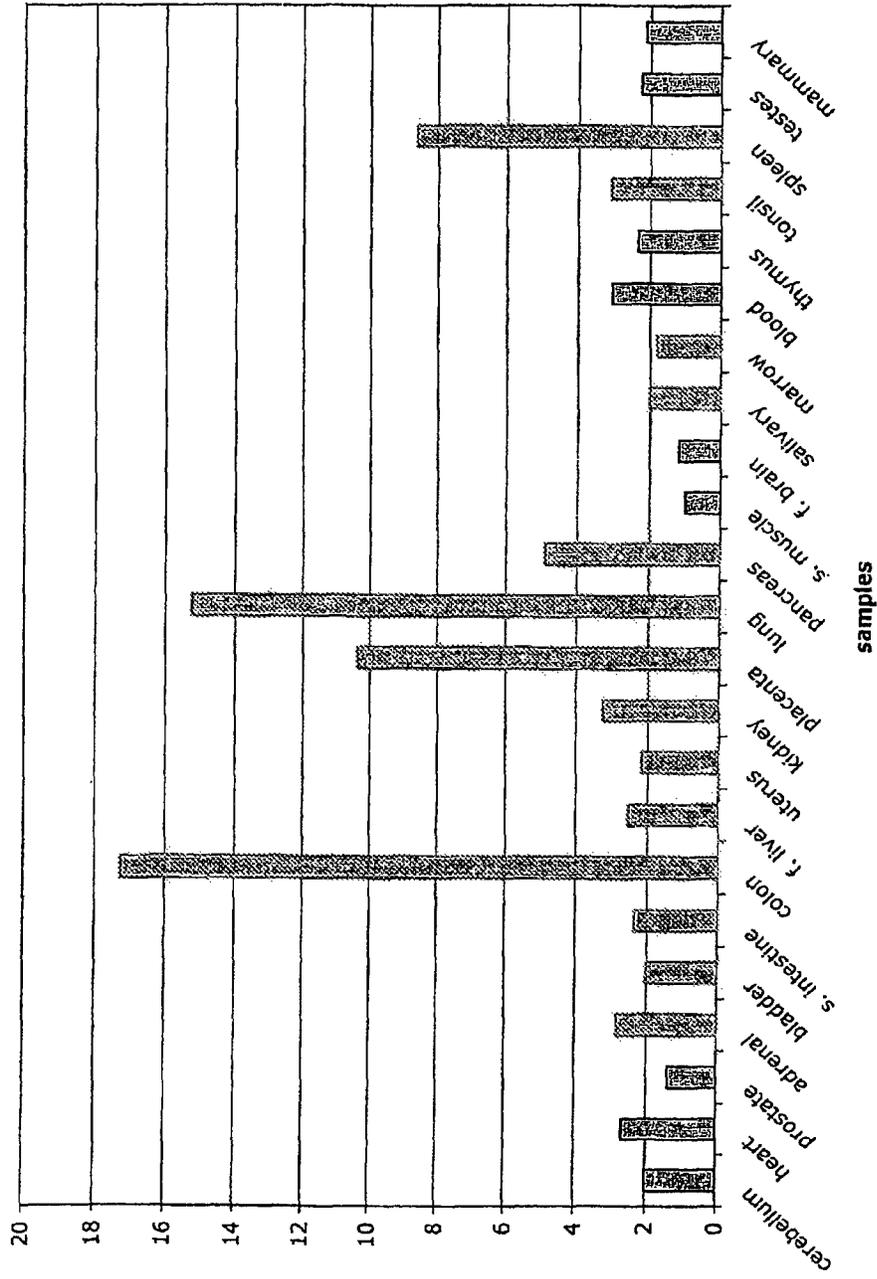


sample

FIGURE 88A

TAHO20/DNA257955/FcRH3

FCRH3

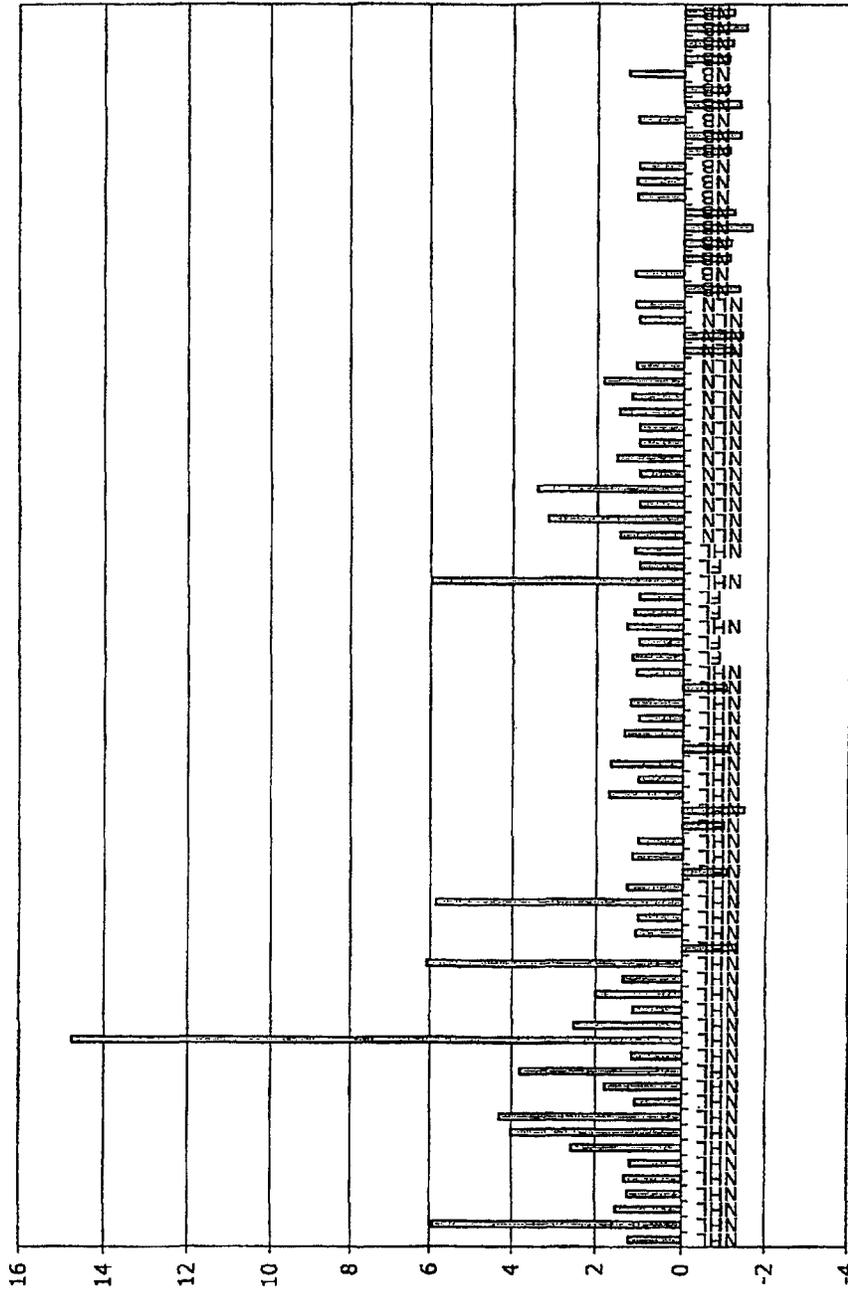


samples

FIGURE 88B

TAHO21/DNA329863/IRTA1

IRTA1

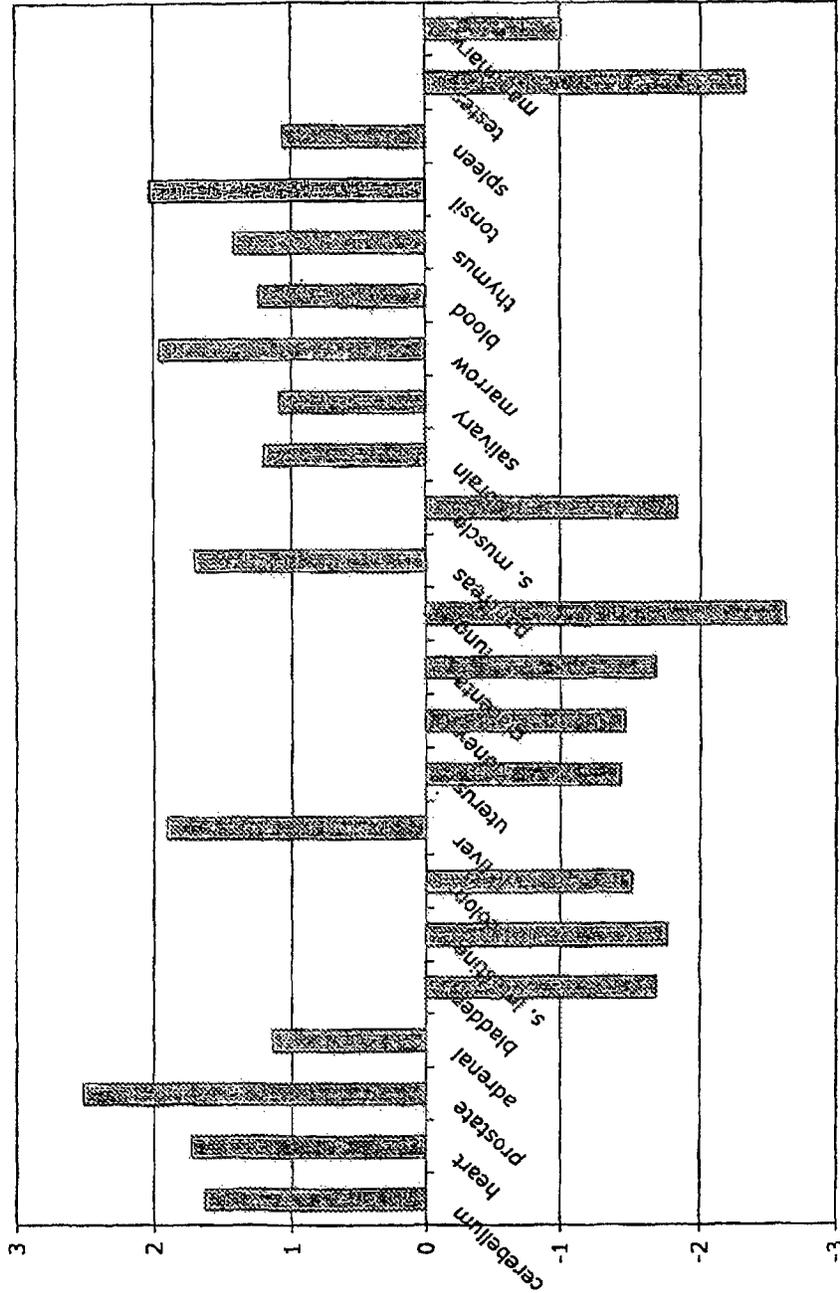


sample

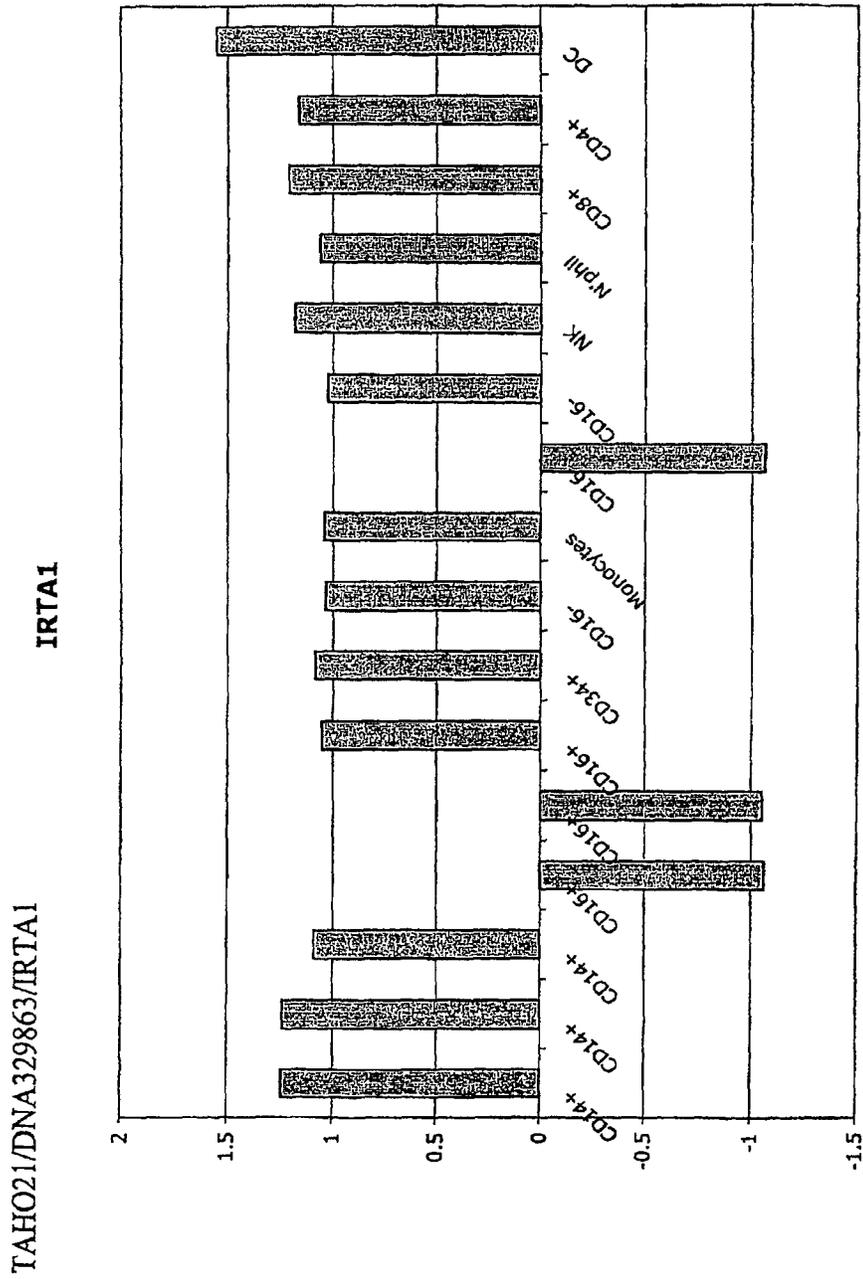
FIGURE 89A

IRTA1

TAHO21/DNA329863/IRTA1



samples
FIGURE 89B



sample
FIGURE 89C

TAHO21/DNA329863/IRTA1

IRTA1

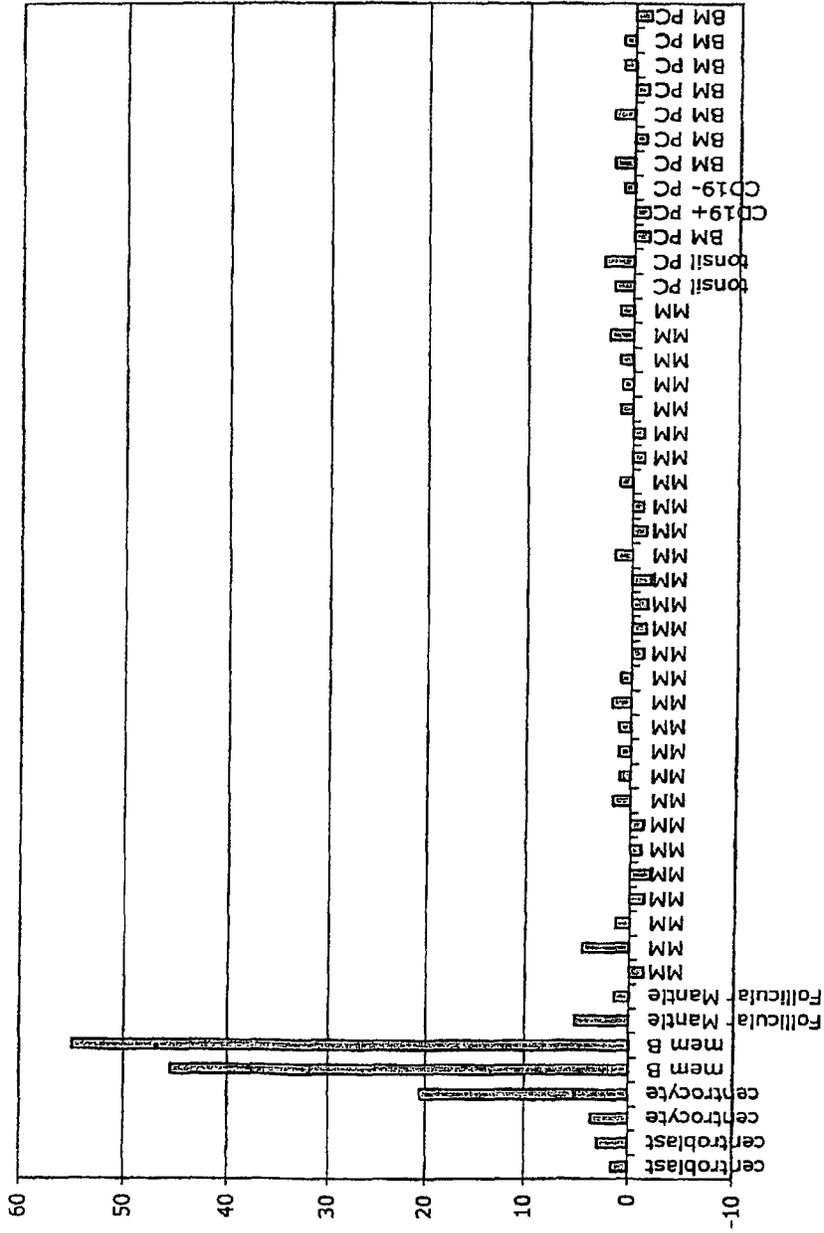
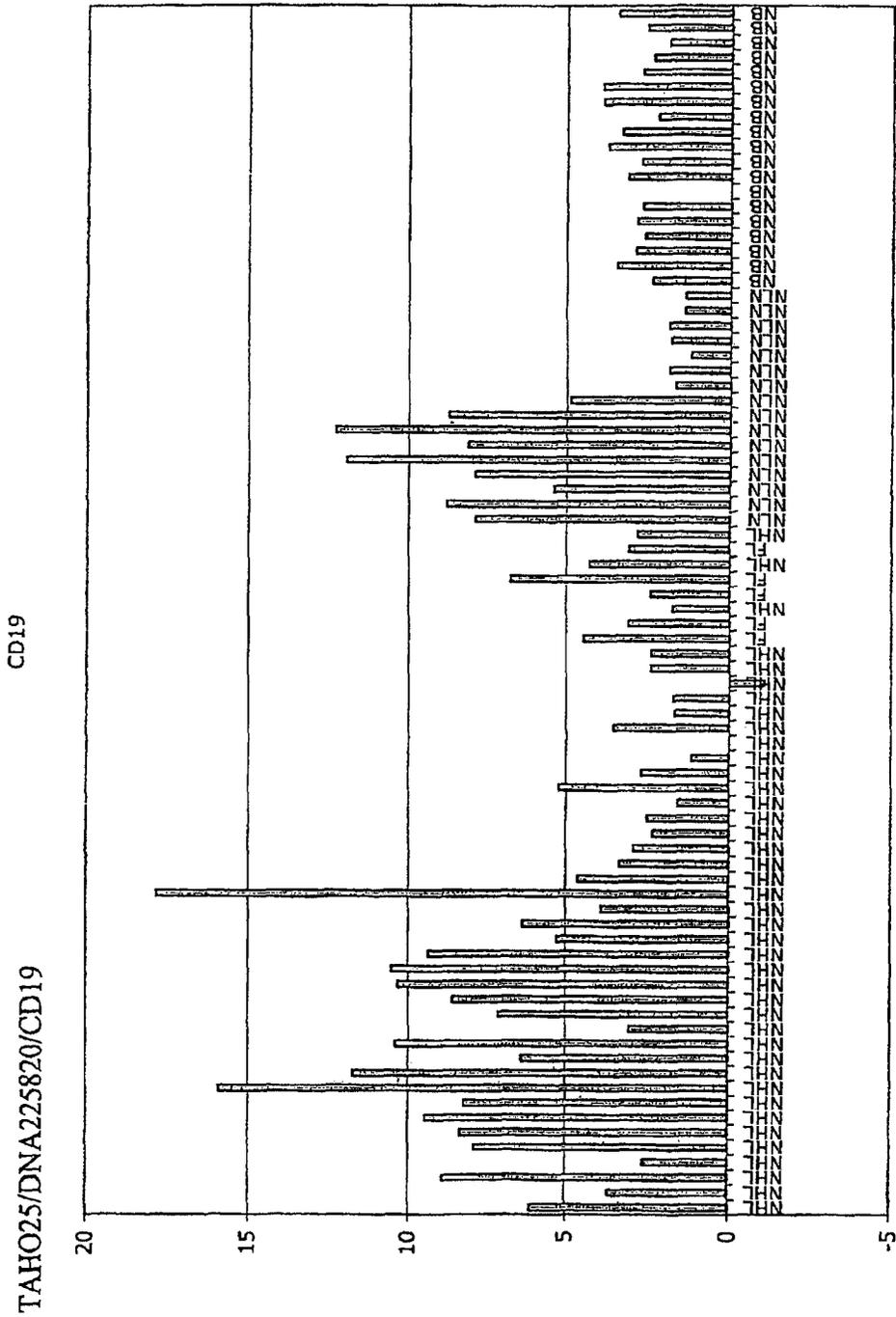
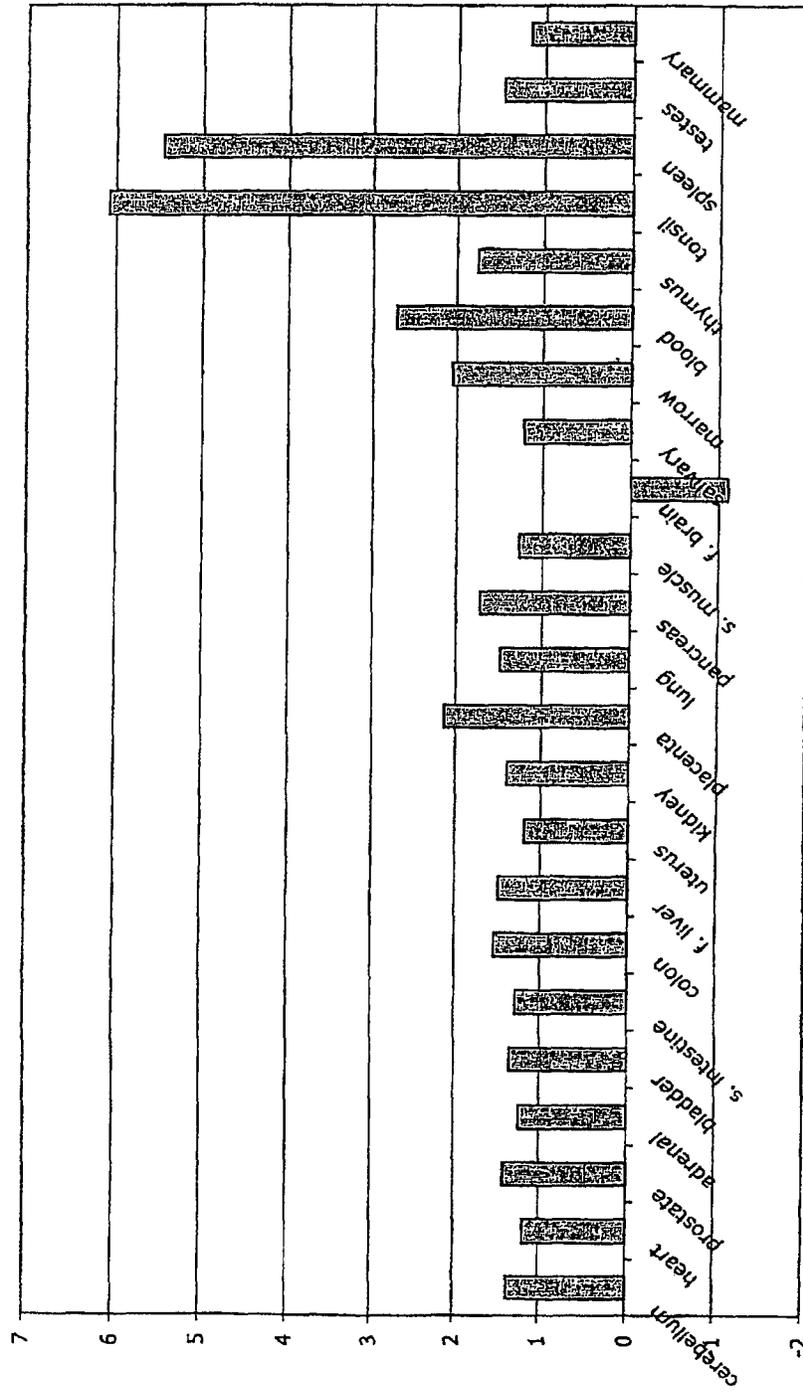


FIGURE 89D



TAHO25/DNA225820/CD19



samples
FIGURE 90B

CD19

TAHO25/DNA225820/CD19

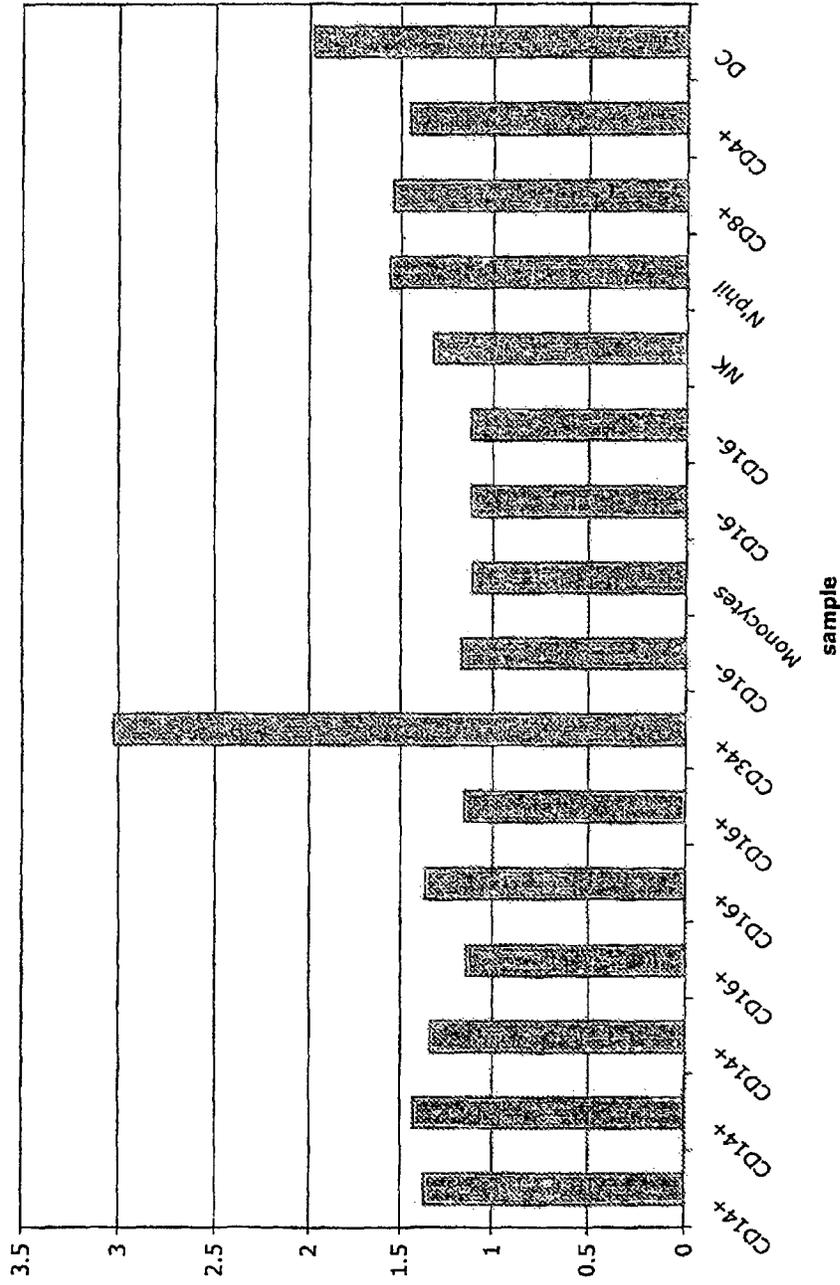
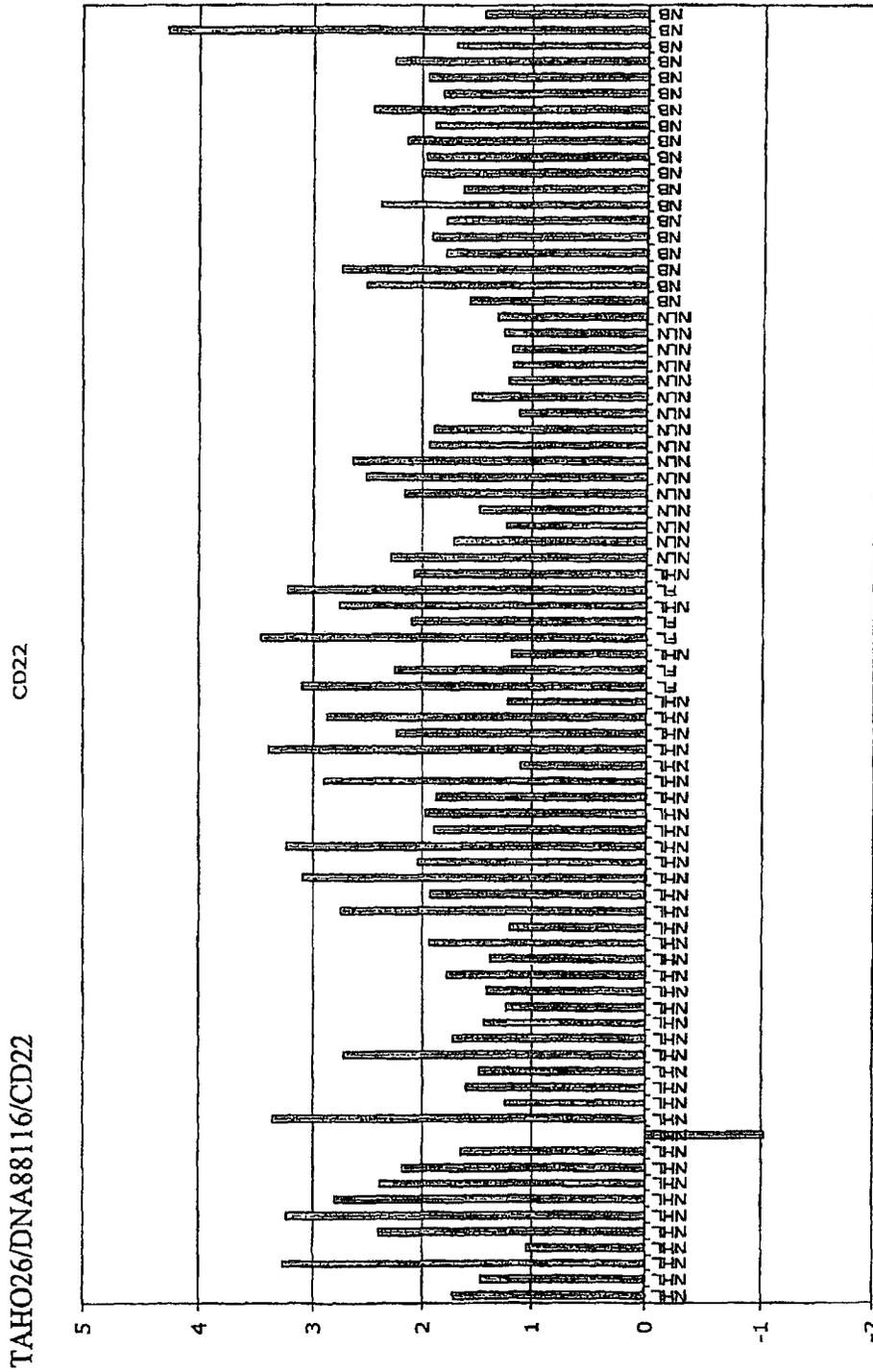
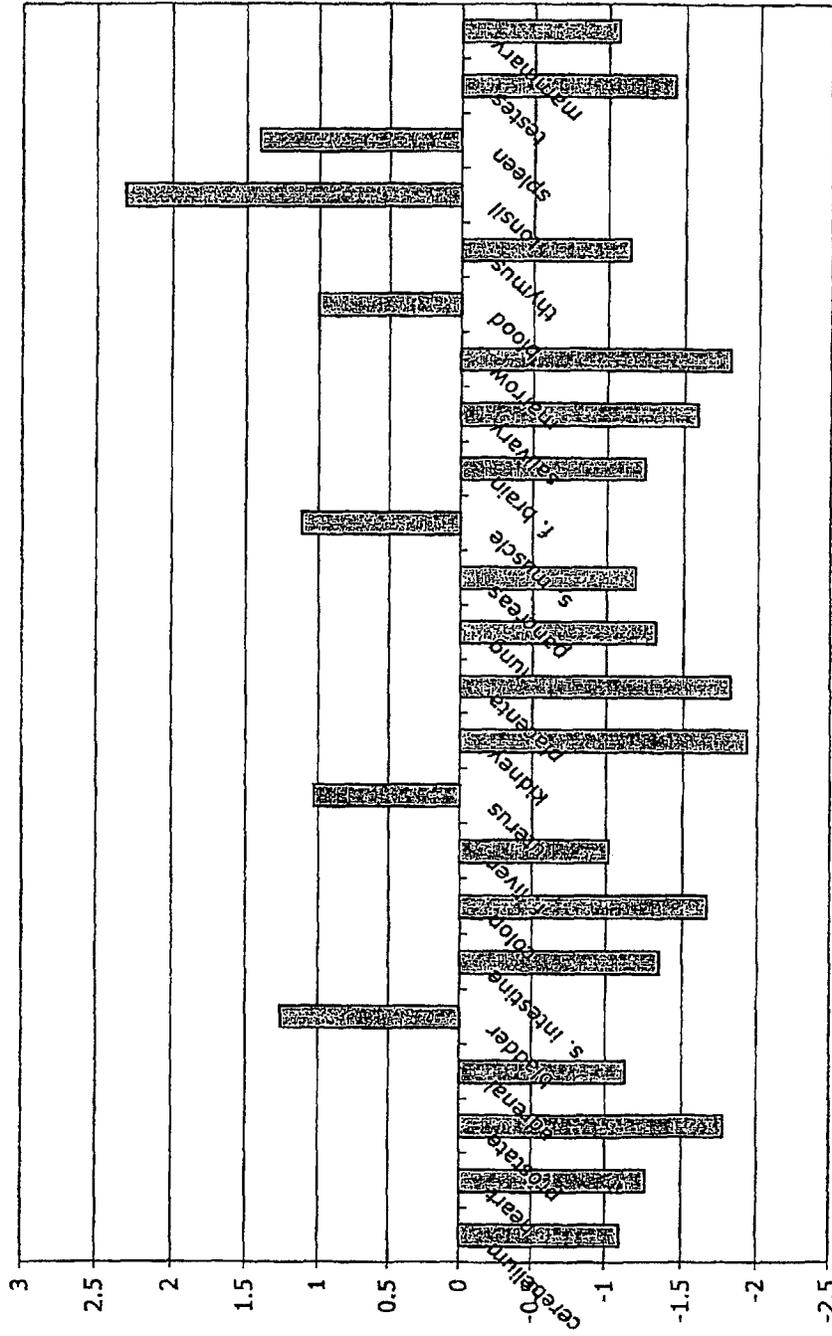


FIGURE 90C



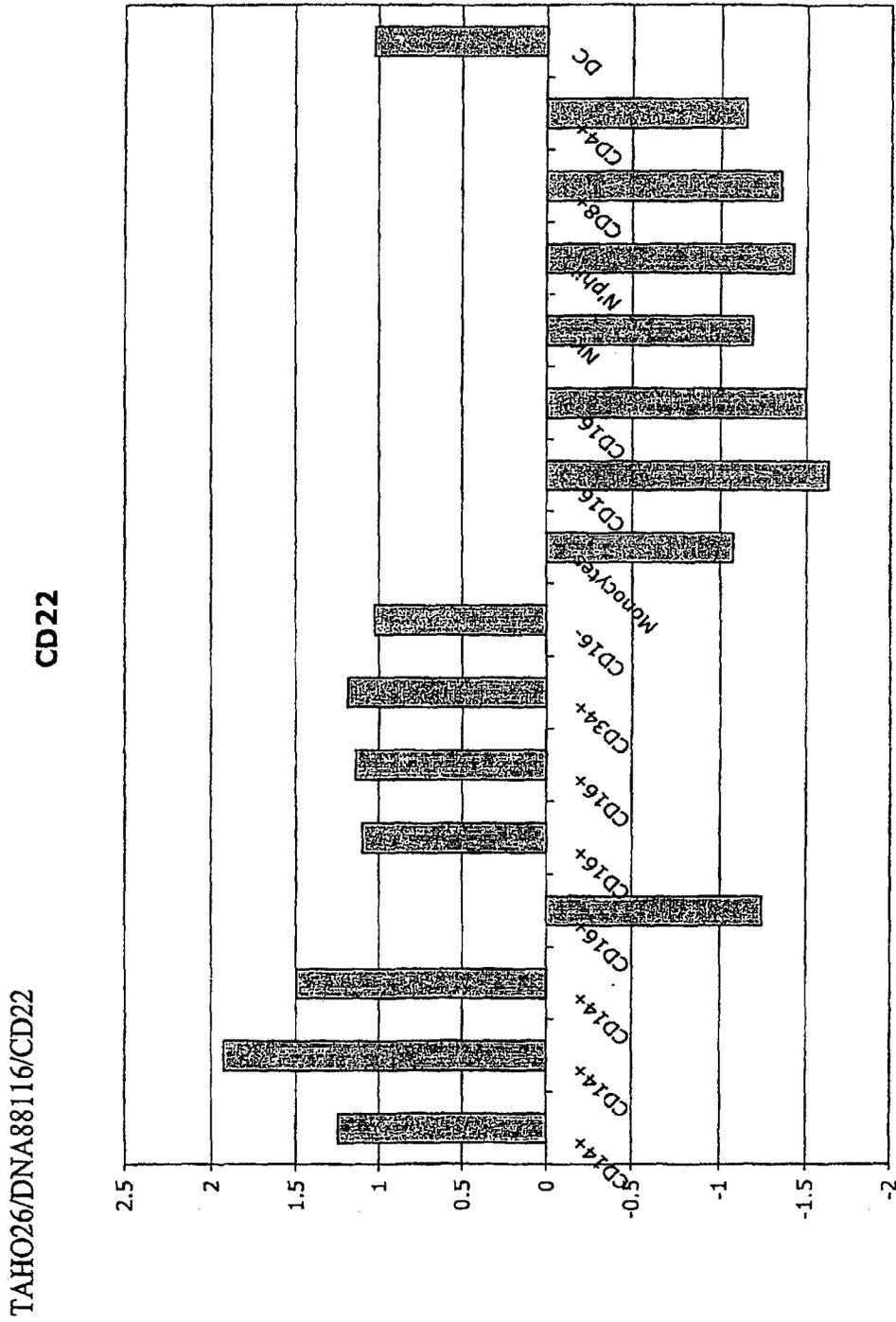
CD22

TAHO26/DNA88116/CD22



samples

FIGURE 91B



sample
FIGURE 91C

TAHO27/DNA227752/CXCR3

CXCR3

UNQ8371

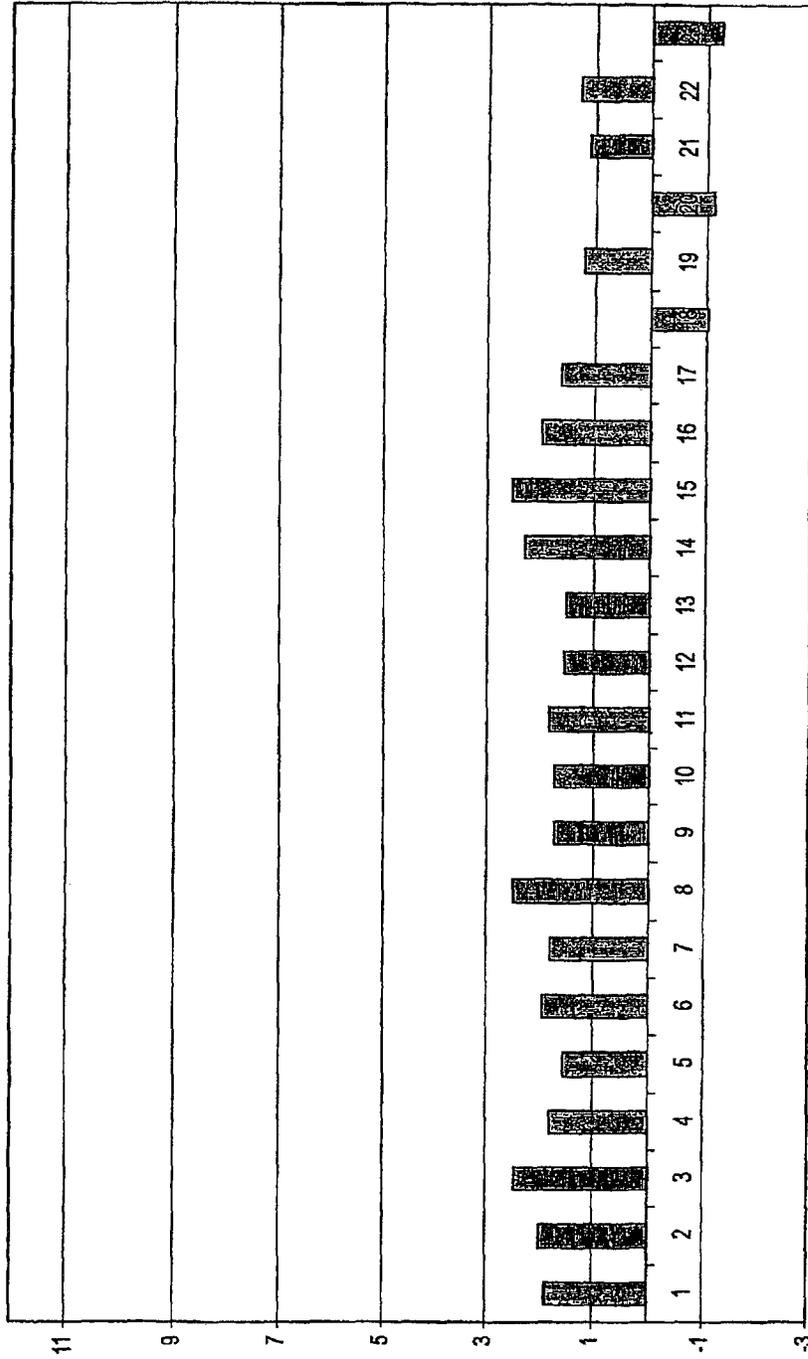


FIGURE 92A

TAHO27/DNA227752/CXCR3

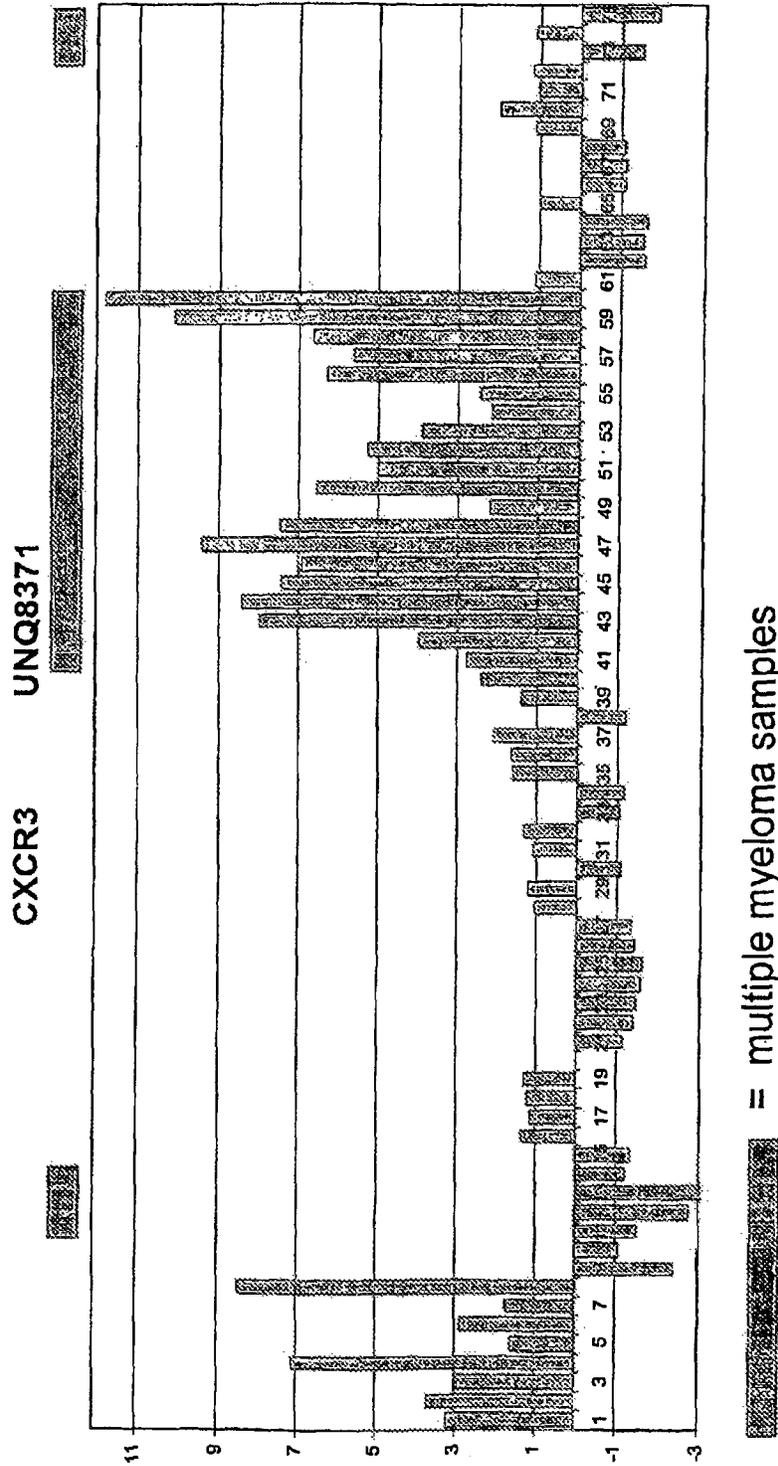


FIGURE 92B

TAHO28/DNA119476/SILV

SILV UNQ1747 gp100=melanocyte lineage-specific antigen/Pmel17 homolog [human, mRNA, 2130 nt]

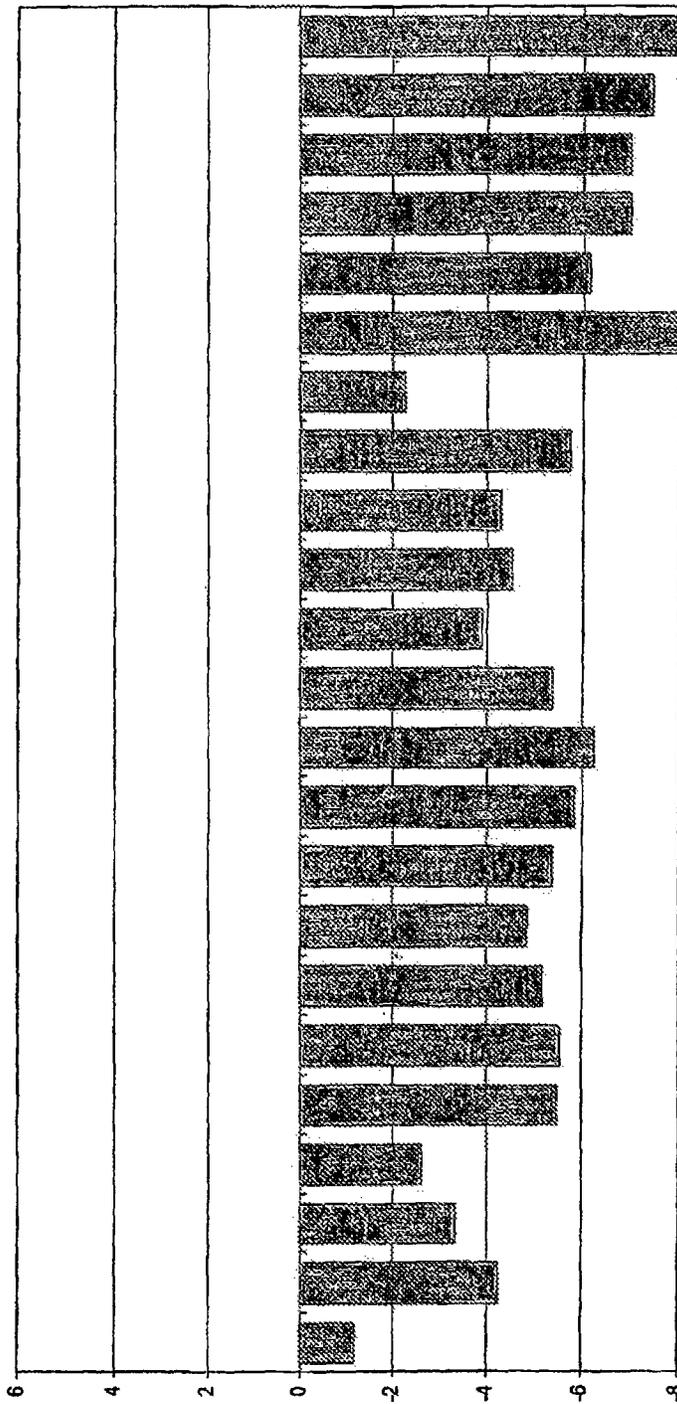


FIGURE 93A

TAHO28/DNA119476/SILV

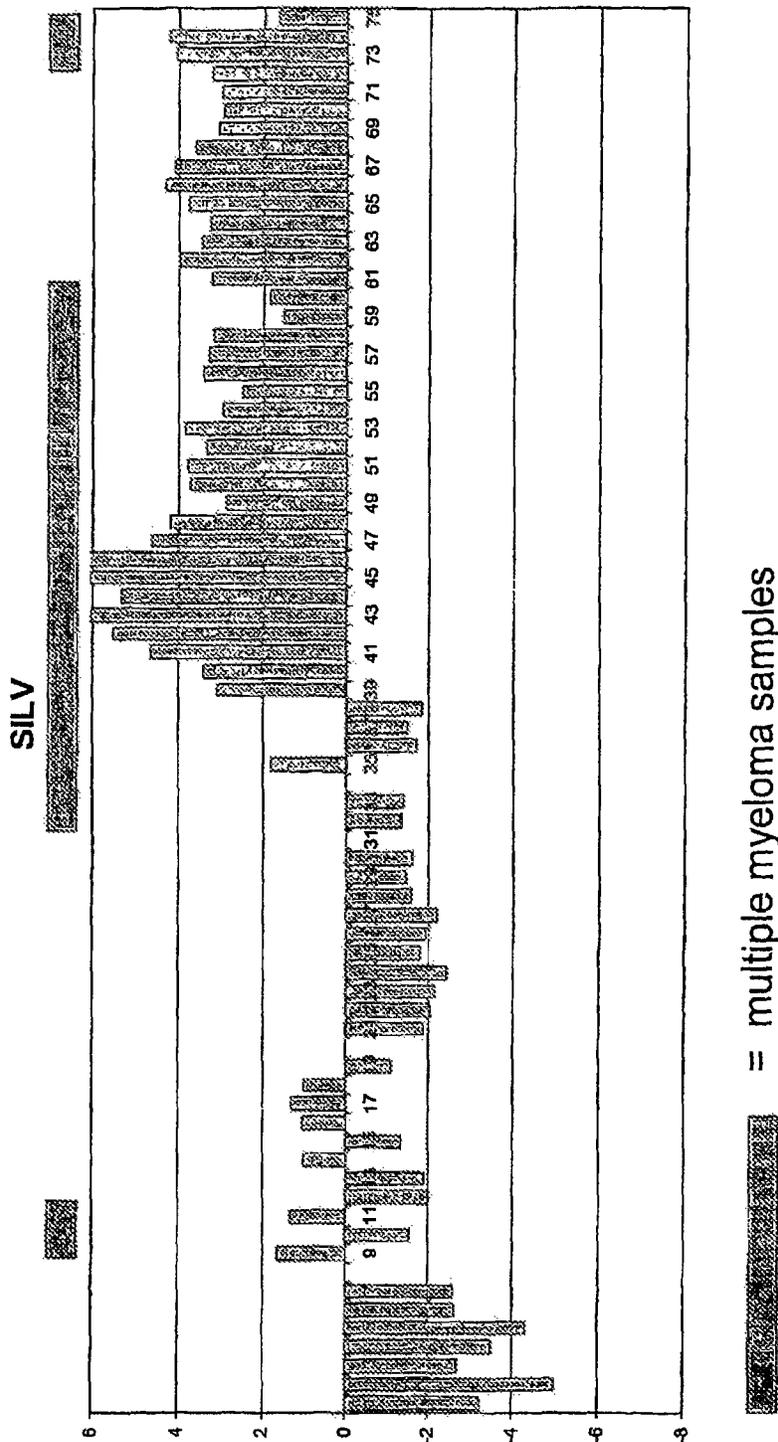


FIGURE 93B

TAHO29/DNA254890/KCNK4

KCNK4 UNQ11492

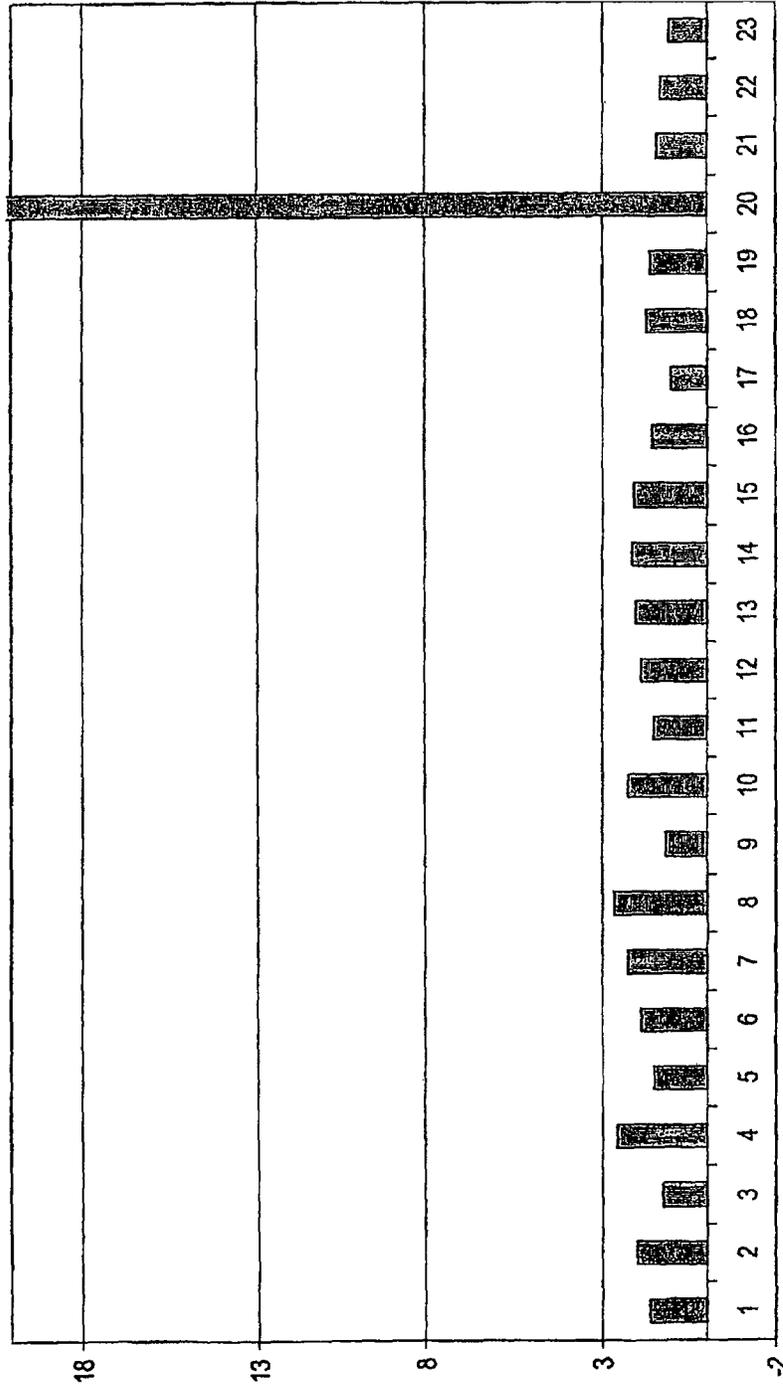


FIGURE 94A

TAHO29/DNA254890/KCNK4

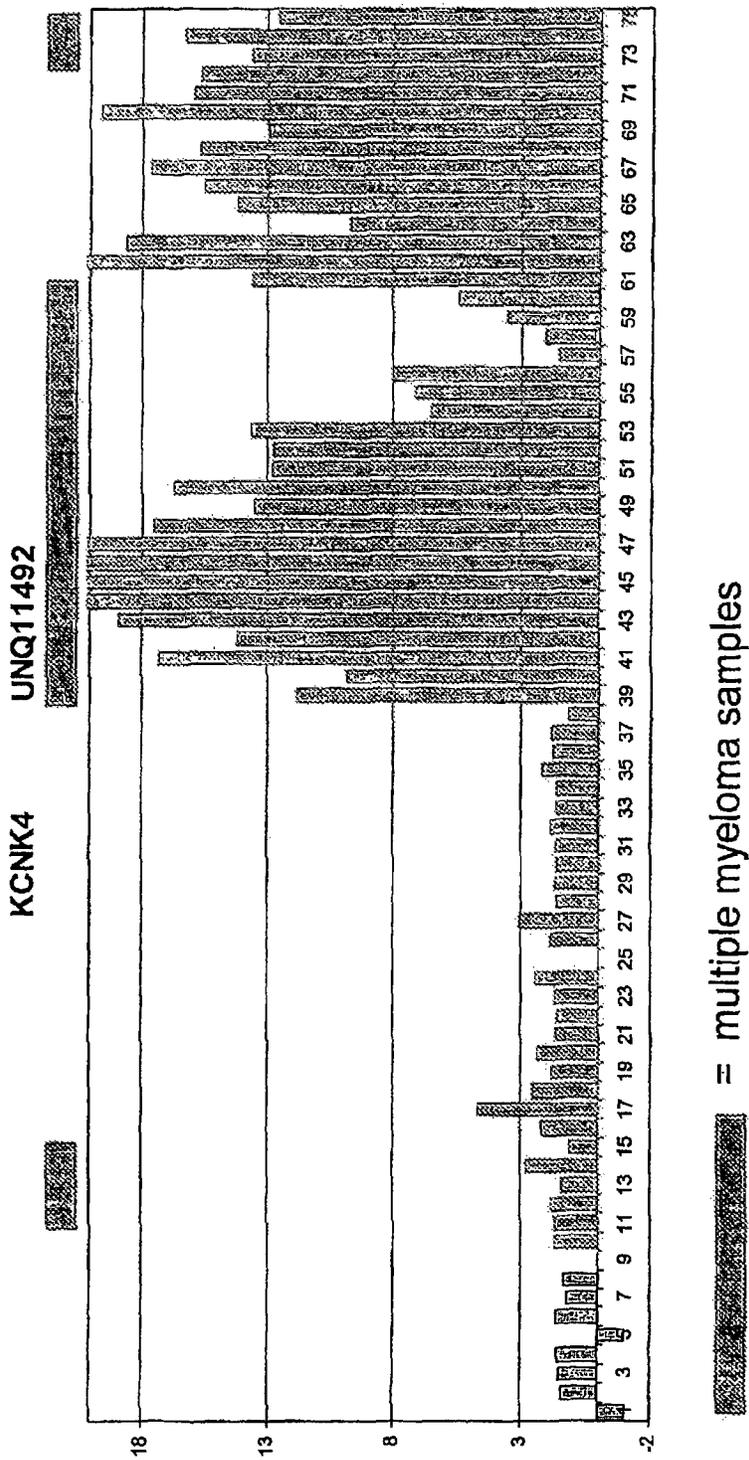


FIGURE 94B



FIGURE 95A

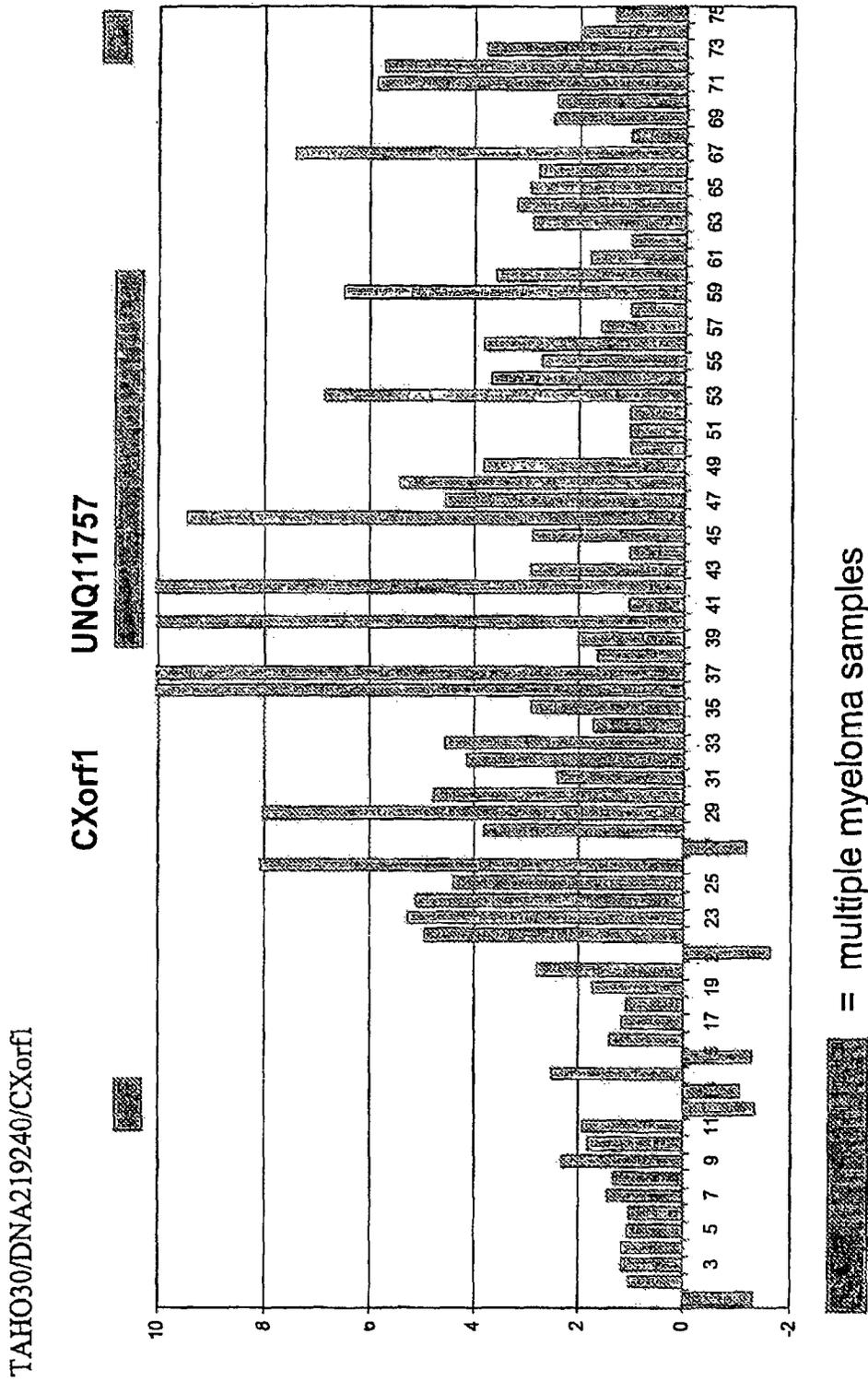


FIGURE 95B

TAHO31/DNA37151/LRRN5

LRRN5 UNQ256

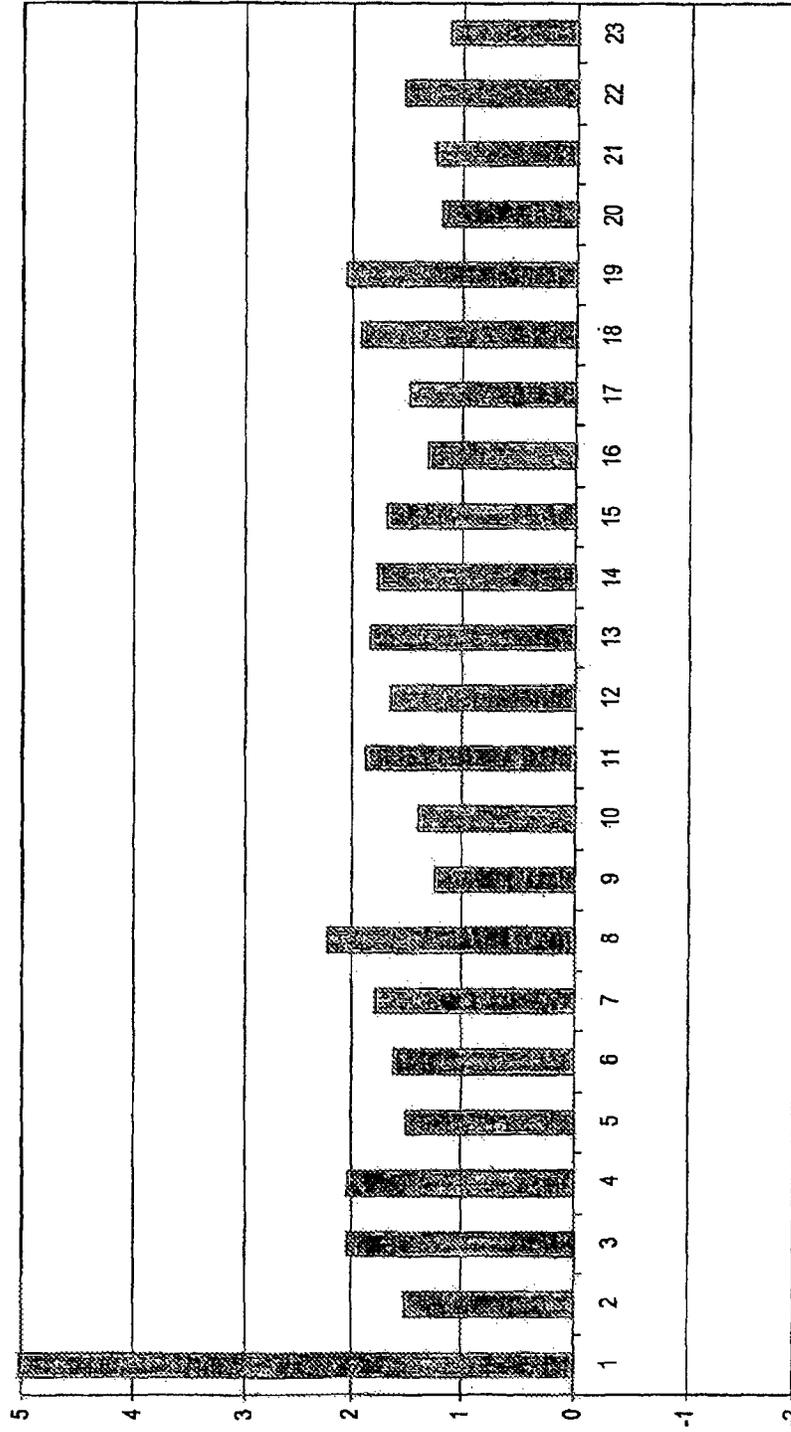
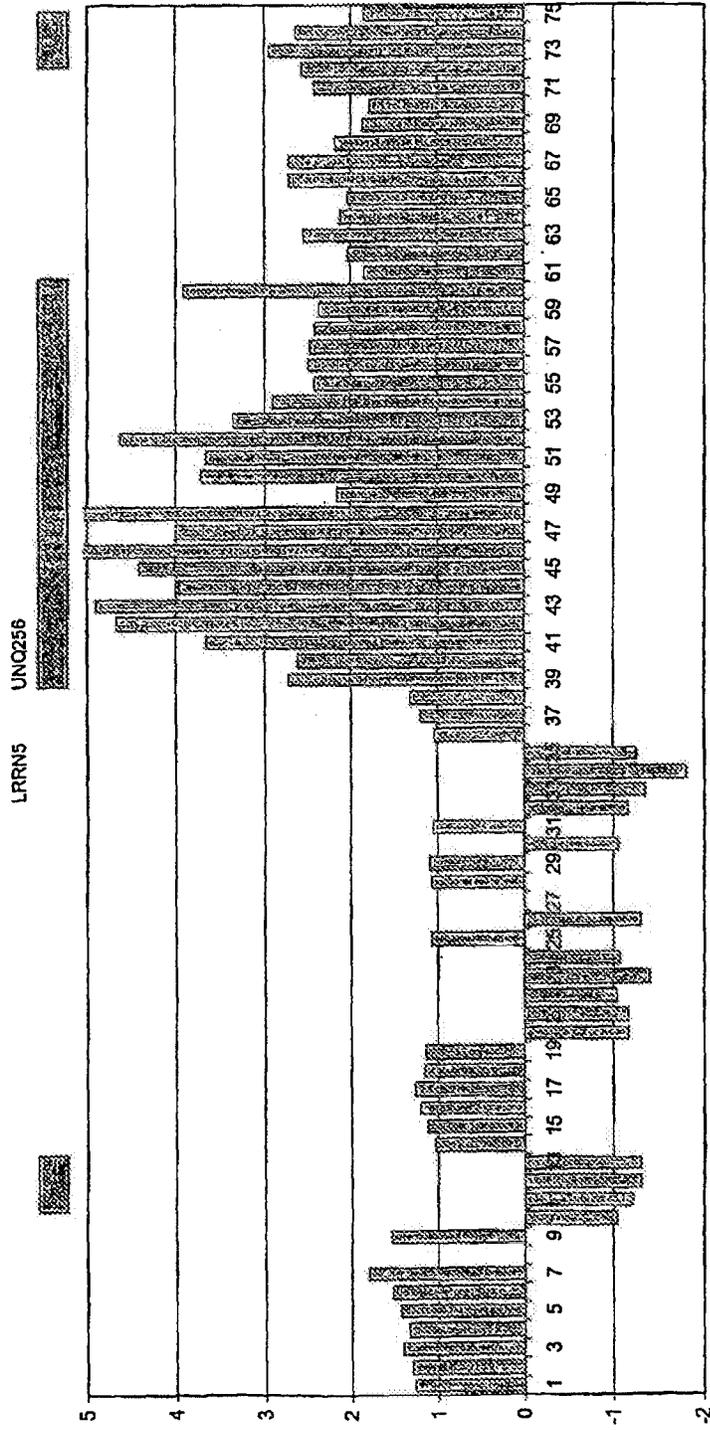


FIGURE 96A

TAHO31/DNA37151/LRRN5



= multiple myeloma samples

FIGURE 96B

TAHO32/DNA210233/UNQ9308

UNQ9308 UNQ9308

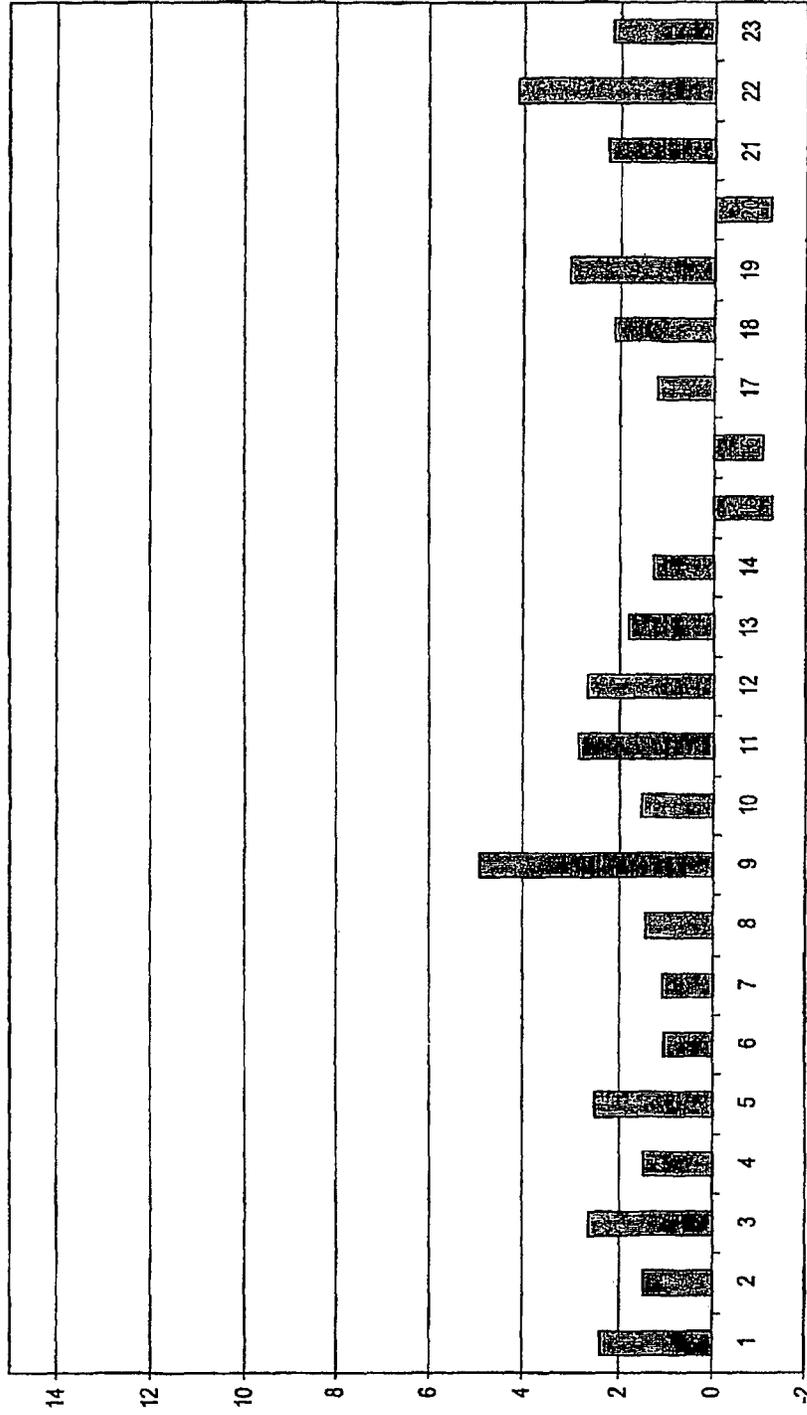
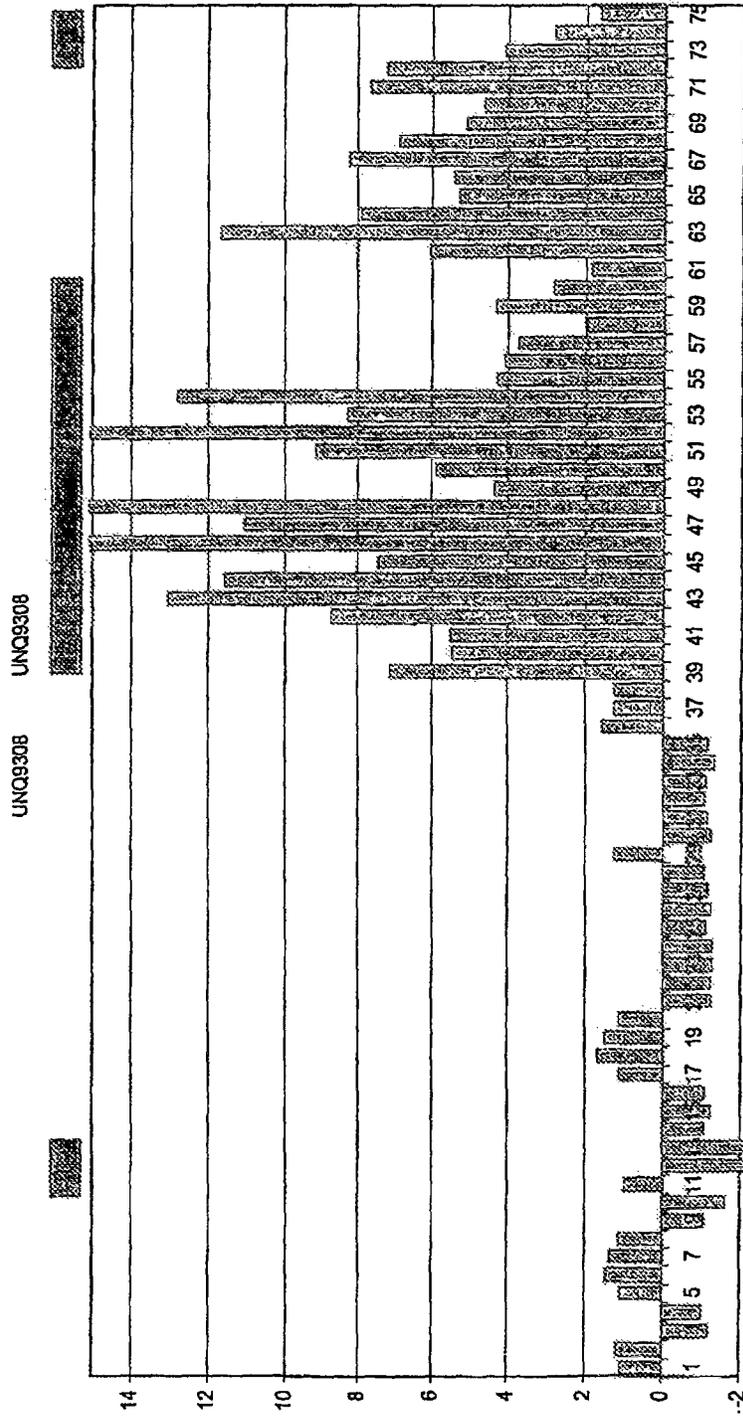


FIGURE 97A

TAHO32/DNA210233/UNO9308
TAHO34/DNA260038/UNQ13267



= multiple myeloma samples

FIGURE 97B

TAHO33/DNA35918/IGSF4B

IGSF4B UNC225

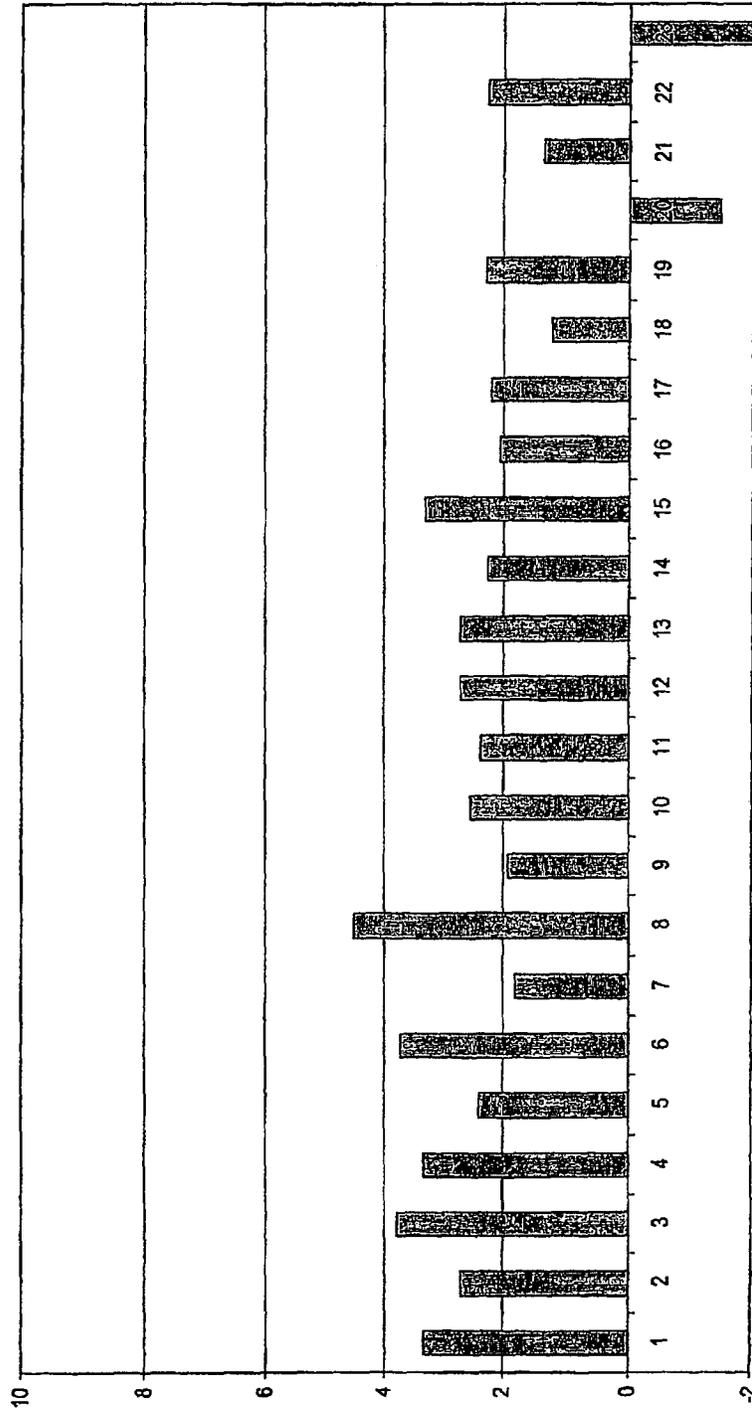


FIGURE 98A

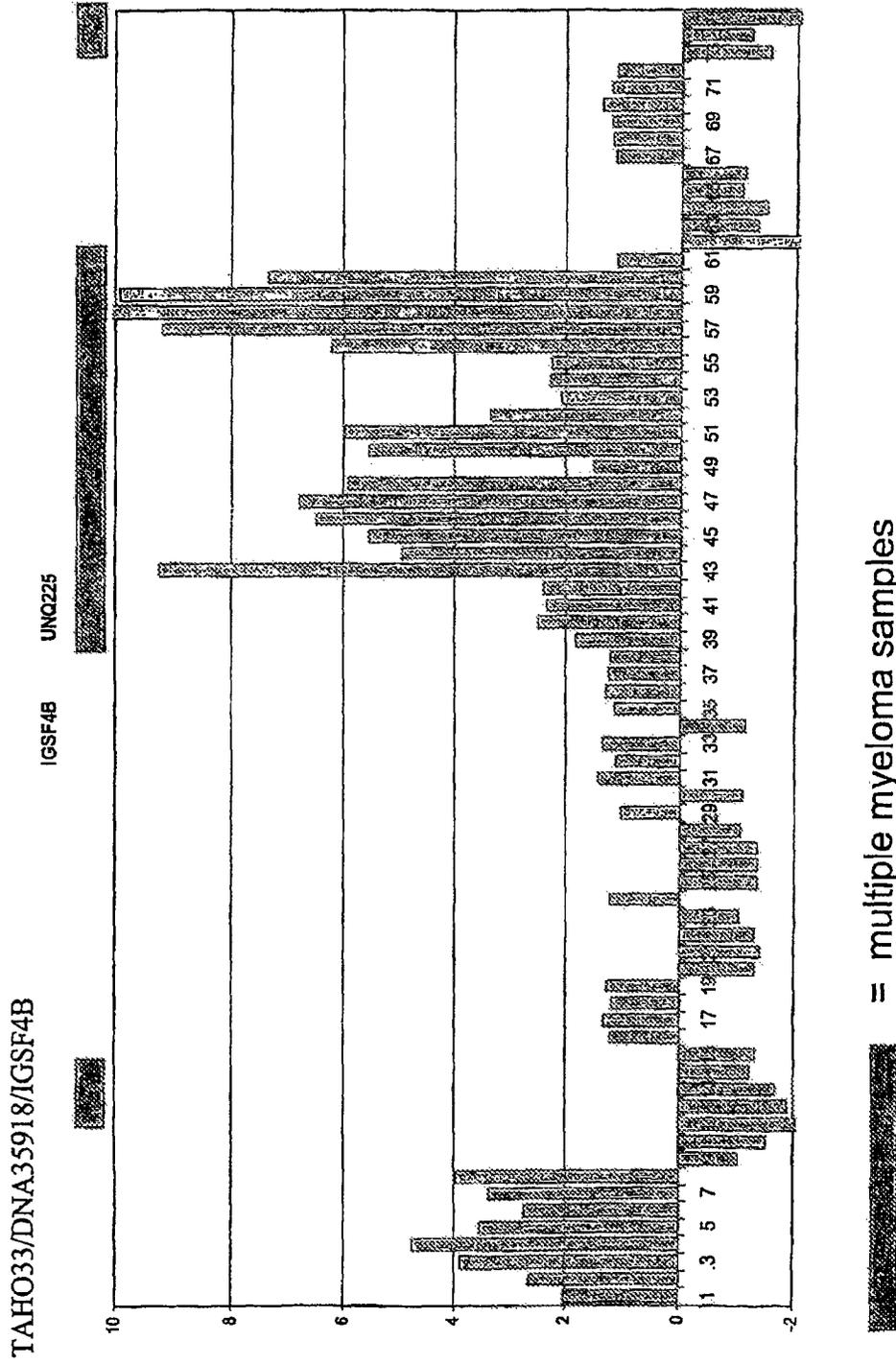


FIGURE 98B

TAHO34/DNA260038/UNQ13267

BC021178 UNQ13267

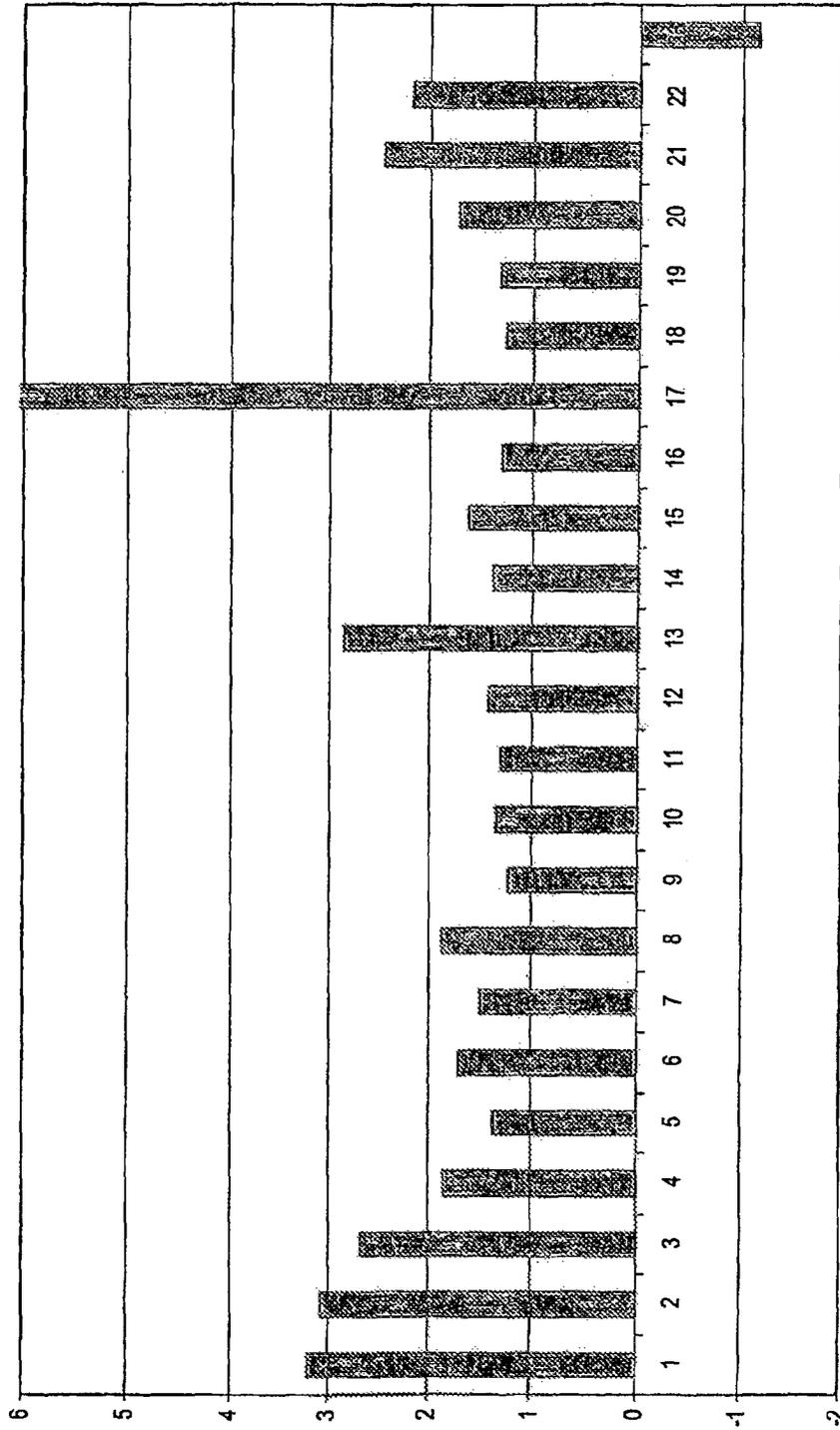


FIGURE 99A

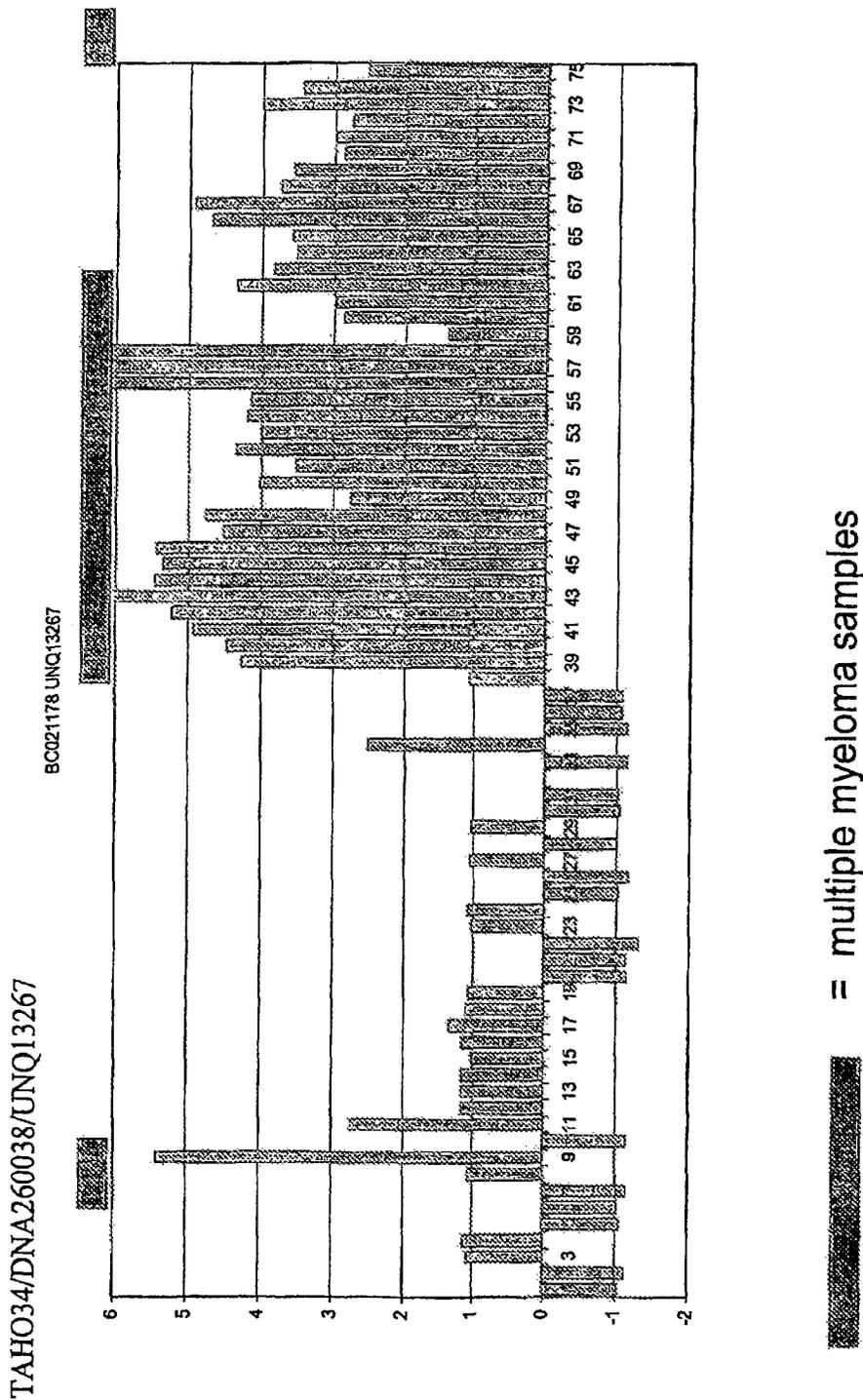


FIGURE 99B

TAHO35/DNA334818/FLJ12681

FLJ12681 UNQ6034

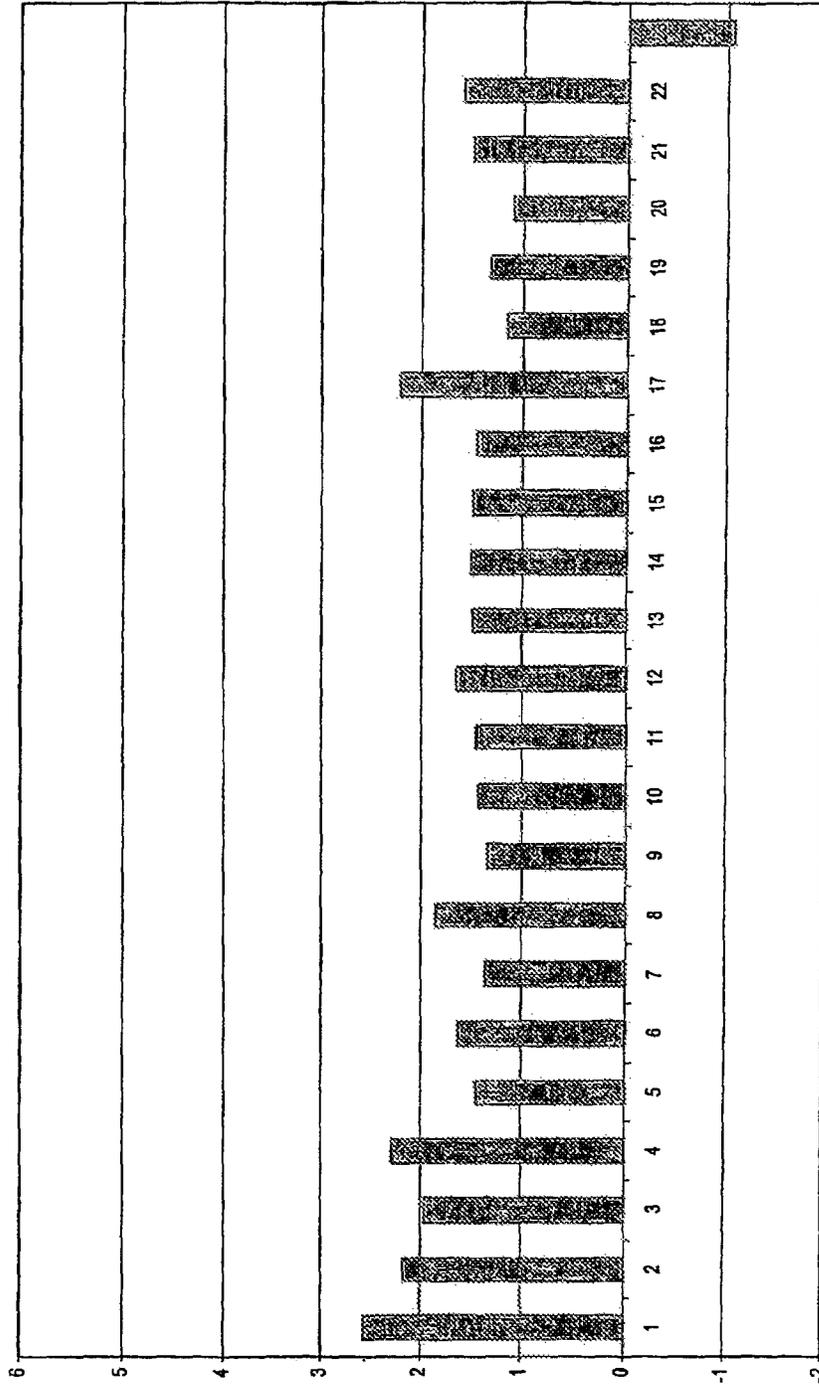


FIGURE 100A

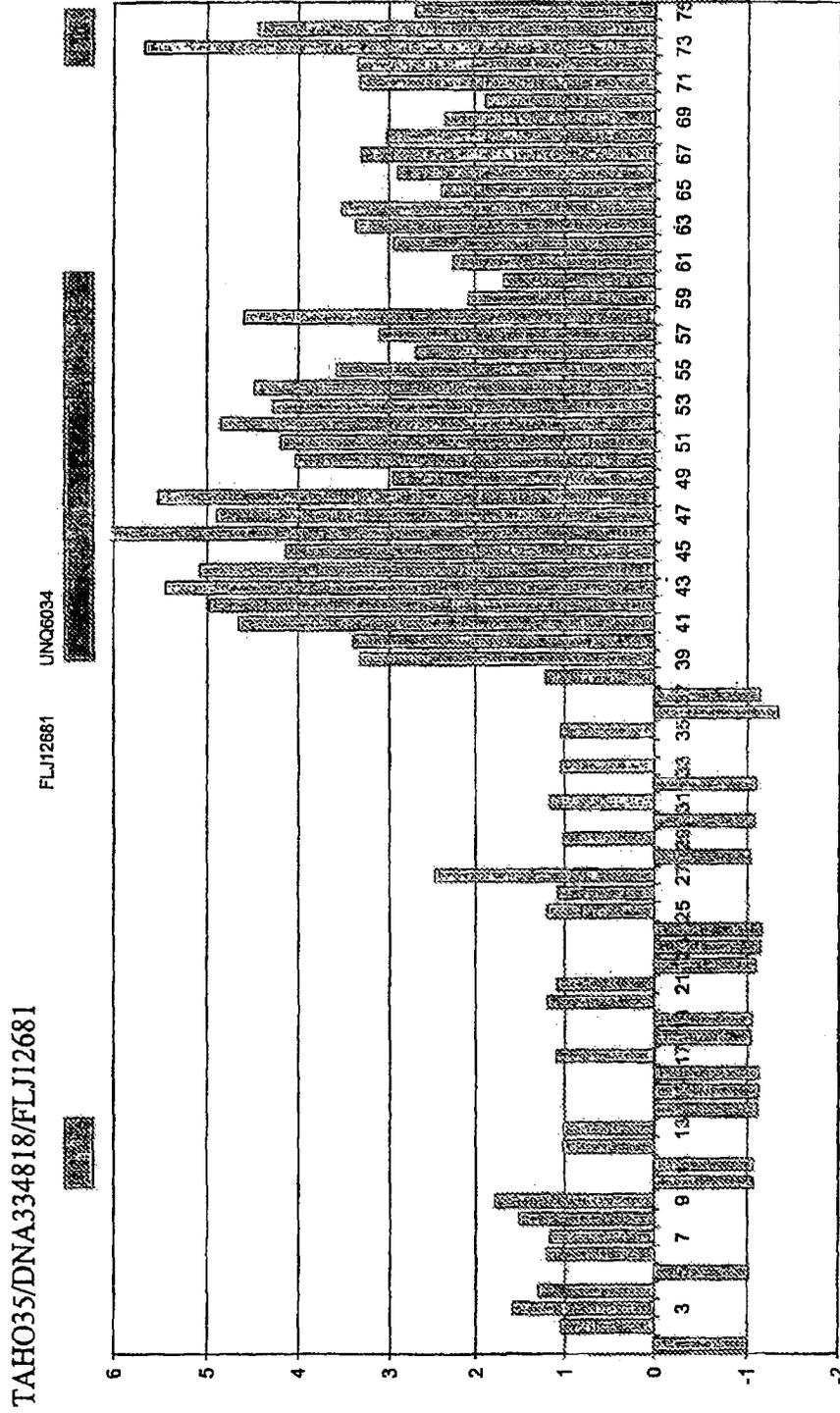


FIGURE 100B

TAHO36/DNA257501/UNQ12376 (I_928646)

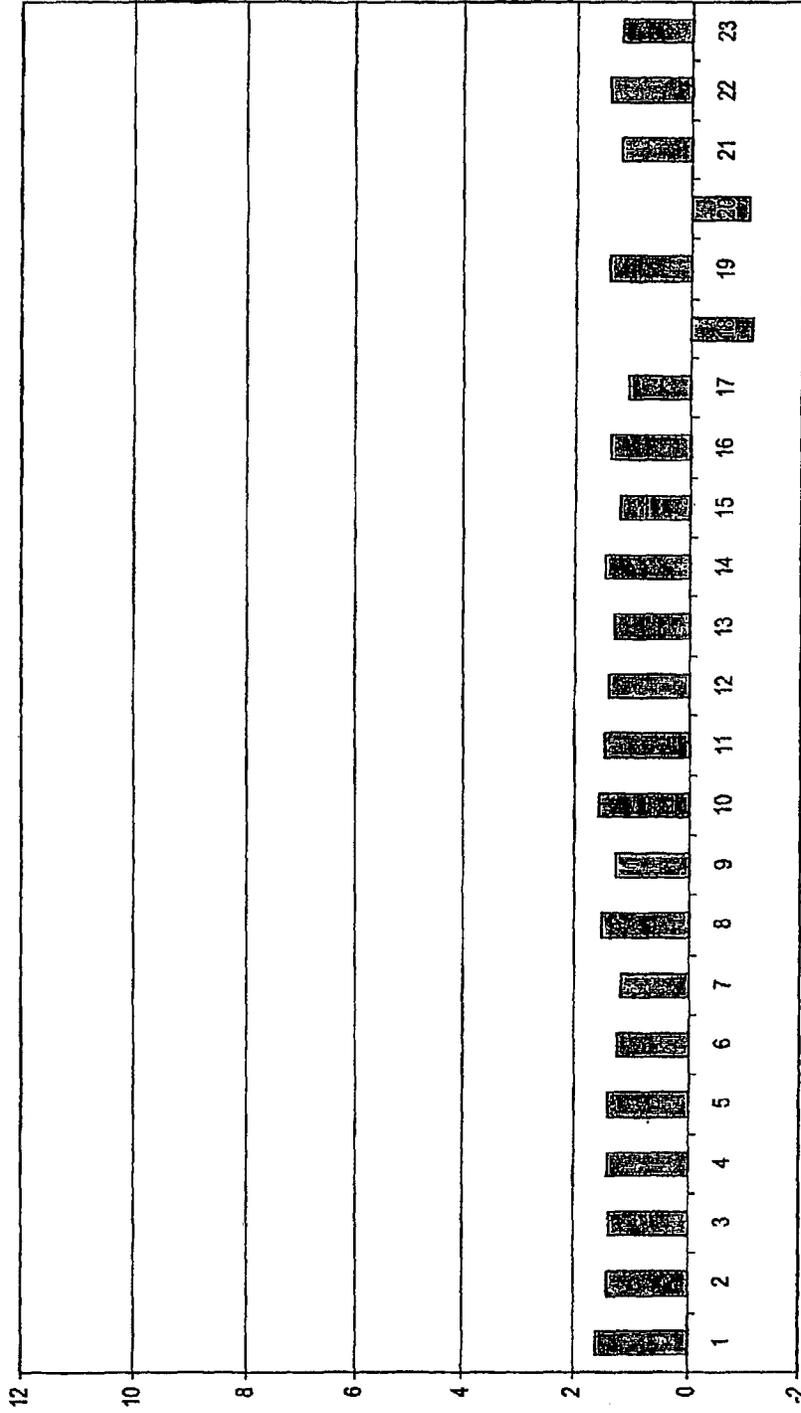
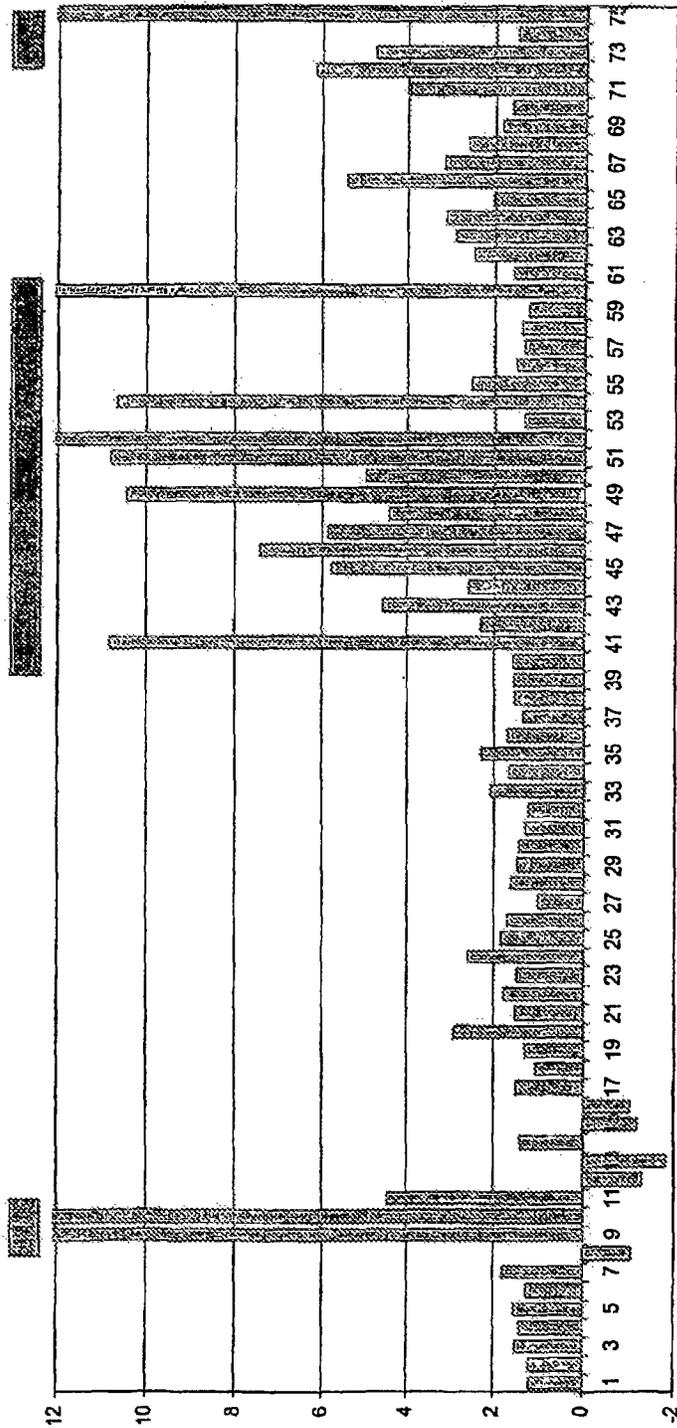


FIGURE 101A

TAHO36/DNA257501/JUNQ12376/I_928646

I_928646



= multiple myeloma samples

FIGURE 101B

COMPOSITIONS AND METHODS FOR THE TREATMENT OF TUMOR OF HEMATOPOIETIC ORIGIN

RELATED APPLICATIONS

The present application is a continuation of, and claims priority under 35 USC §120 to U.S. application Ser. No. 12/756,149, filed Apr. 7, 2010, now abandoned which is a continuation of, and claims priority under 35 USC §120 to U.S. application Ser. No. 12/079,893, filed Mar. 27, 2008, which is a continuation of, and claims priority under 35 U.S.C. §120 to U.S. application Ser. No. 10/989,826, filed Nov. 16, 2004, now abandoned which is a continuation-in-part of, and claims priority under 35 USC §120 to both, PCT Application PCT/US03/36298, filed Nov. 13, 2003 and also to U.S. application Ser. No. 10/712,892, filed Nov. 12, 2003, now abandoned both of which claim priority under 35 USC §119 to U.S. Provisional Application 60/405,645, filed Aug. 21, 2002 and also to 60/426,847, filed Nov. 15, 2002, and wherein PCT Application PCT/US03/36298, filed Nov. 13, 2003 and U.S. application Ser. No. 10/712,892, filed Nov. 13, 2003 are also both continuations-in-part of, and claim priority under 35 USC §120 to both, PCT Application PCT/US03/25892, filed Aug. 19, 2003 and also to U.S. application Ser. No. 10/643,795, filed Aug. 19, 2003, both of which claim priority under 35 USC §119 to U.S. Provisional Application 60/404,809, filed Aug. 19, 2002, and also to 60/405,645, filed Aug. 21, 2002, and wherein PCT Application PCT/US03/25892, filed Aug. 19, 2003 and U.S. application Ser. No. 10/643,795, filed Aug. 19, 2003, both of which are also continuations-in-part of, and claim priority under 35 USC §120 to both PCT Application PCT/US03/11148, filed Apr. 10, 2003 and also to U.S. application Ser. No. 10/411,010, filed Apr. 10, 2003, both of which claim priority under 35 USC §119 to U.S. Provisional Applications, 60/378,885, filed May 8, 2002, and also to 60/404,809, filed Aug. 19, 2002, and wherein PCT Application PCT/US03/11148, filed Apr. 10, 2003 and U.S. application Ser. No. 10/411,010, filed Apr. 10, 2003, both of which are also continuations-in-part of, and claim priority under 35 USC §120 to both, PCT Application PCT/US02/28859, filed Sep. 11, 2002 and also to U.S. application Ser. No. 10/241,220, filed Sep. 11, 2002, both of which claim priority under 35 USC §119 to U.S. Provisional Application 60/339,227, filed Oct. 19, 2001, and wherein PCT Application PCT/US02/28859, filed Sep. 11, 2002 and U.S. application Ser. No. 10/241,220, filed Sep. 11, 2002, both of which are also continuations-in-part of, and claim priority under 35 USC §120 to both, PCT/US02/12206, filed Apr. 17, 2002 and also to U.S. application Ser. No. 10/125,166, filed Apr. 17, 2002, and wherein the present application also claims priority under 35 USC §119 to U.S. Provisional Application 60/520,842, filed Nov. 17, 2003, and also to U.S. Provisional Application 60/532,426, filed Dec. 24, 2003, and also to U.S. Provisional Application 60/576,517, filed Jun. 1, 2004, and also to U.S. Provisional Application 60/616,098, filed Oct. 5, 2004.

FIELD OF THE INVENTION

The present invention is directed to compositions of matter useful for the treatment of hematopoietic tumor in mammals and to methods of using those compositions of matter for the same.

BACKGROUND OF THE INVENTION

Malignant tumors (cancers) are the second leading cause of death in the United States, after heart disease (Boring et al.,

CA Cancel J. Clin. 43:7 (1993)). Cancer is characterized by the increase in the number of abnormal, or neoplastic, cells derived from a normal tissue which proliferate to form a tumor mass, the invasion of adjacent tissues by these neoplastic tumor cells, and the generation of malignant cells which eventually spread via the blood or lymphatic system to regional lymph nodes and to distant sites via a process called metastasis. In a cancerous state, a cell proliferates under conditions in which normal cells would not grow. Cancer manifests itself in a wide variety of forms, characterized by different degrees of invasiveness and aggressiveness.

Cancers which involve cells generated during hematopoiesis, a process by which cellular elements of blood, such as lymphocytes, leukocytes, platelets, erythrocytes and natural killer cells are generated are referred to as hematopoietic cancers. Lymphocytes which can be found in blood and lymphatic tissue and are critical for immune response are categorized into two main classes of lymphocytes: B lymphocytes (B cells) and T lymphocytes (T cells), which mediate humoral and cell mediated immunity, respectively.

B cells mature within the bone marrow and leave the marrow expressing an antigen-binding antibody on their cell surface. When a naive B cell first encounters the antigen for which its membrane-bound antibody is specific, the cell begins to divide rapidly and its progeny differentiate into memory B cells and effector cells called "plasma cells". Memory B cells have a longer life span and continue to express membrane-bound antibody with the same specificity as the original parent cell. Plasma cells do not produce membrane-bound antibody but instead produce the antibody in a form that can be secreted. Secreted antibodies are the major effector molecule of humoral immunity.

T cells mature within the thymus which provides an environment for the proliferation and differentiation of immature T cells. During T cell maturation, the T cells undergo the gene rearrangements that produce the T-cell receptor and the positive and negative selection which helps determine the cell-surface phenotype of the mature T cell. Characteristic cell surface markers of mature T cells are the CD3:T-cell receptor complex and one of the coreceptors, CD4 or CD8.

In attempts to discover effective cellular targets for cancer therapy, researchers have sought to identify transmembrane or otherwise membrane-associated polypeptides that are specifically expressed on the surface of one or more particular type(s) of cancer cell as compared to on one or more normal non-cancerous cell(s). Often, such membrane-associated polypeptides are more abundantly expressed on the surface of the cancer cells as compared to on the surface of the non-cancerous cells. The identification of such tumor-associated cell surface antigen polypeptides has given rise to the ability to specifically target cancer cells for destruction via antibody-based therapies. In this regard, it is noted that antibody-based therapy has proved very effective in the treatment of certain cancers. For example, HERCEPTIN® and RITUXAN® (both from Genentech Inc., South San Francisco, Calif.) are antibodies that have been used successfully to treat breast cancer and non-Hodgkin's lymphoma, respectively. More specifically, HERCEPTIN® is a recombinant DNA-derived humanized monoclonal antibody that selectively binds to the extracellular domain of the human epidermal growth factor receptor 2 (HER2) proto-oncogene. HER2 protein overexpression is observed in 25-30% of primary breast cancers. RITUXAN® is a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes. Both these antibodies are recombinantly produced in CHO cells.

In other attempts to discover effective cellular targets for cancer therapy, researchers have sought to identify (1) non-membrane-associated polypeptides that are specifically produced by one or more particular type(s) of cancer cell(s) as compared to by one or more particular type(s) of non-cancerous normal cell(s), (2) polypeptides that are produced by cancer cells at an expression level that is significantly higher than that of one or more normal non-cancerous cell(s), or (3) polypeptides whose expression is specifically limited to only a single (or very limited number of different) tissue type(s) in both the cancerous and non-cancerous state (e.g., normal prostate and prostate tumor tissue). Such polypeptides may remain intracellularly located or may be secreted by the cancer cell. Moreover, such polypeptides may be expressed not by the cancer cell itself, but rather by cells which produce and/or secrete polypeptides having a potentiating or growth-enhancing effect on cancer cells. Such secreted polypeptides are often proteins that provide cancer cells with a growth advantage over normal cells and include such things as, for example, angiogenic factors, cellular adhesion factors, growth factors, and the like. Identification of antagonists of such non-membrane associated polypeptides would be expected to serve as effective therapeutic agents for the treatment of such cancers. Furthermore, identification of the expression pattern of such polypeptides would be useful for the diagnosis of particular cancers in mammals.

Despite the above identified advances in mammalian cancer therapy, there is a great need for additional therapeutic agents capable of detecting the presence of tumor in a mammal and for effectively inhibiting neoplastic cell growth, respectively. Accordingly, it is an objective of the present invention to identify polypeptides, cell membrane-associated, secreted or intracellular polypeptides whose expression is specifically limited to only a single (or very limited number of different) tissue type(s), hematopoietic tissues, in both a cancerous and non-cancerous state, and to use those polypeptides, and their encoding nucleic acids, to produce compositions of matter useful in the therapeutic treatment detection of hematopoietic cancer in mammals.

SUMMARY OF THE INVENTION

A. Embodiments

In the present specification, Applicants describe for the first time the identification of various cellular polypeptides (and their encoding nucleic acids or fragments thereof) which are specifically expressed by both tumor and normal cells of a specific cell type, for example cells generated during hematopoiesis, i.e. lymphocytes, leukocytes, erythrocytes and platelets. All of the above polypeptides are herein referred to as Tumor Antigens of Hematopoietic Origin polypeptides ("TAHO" polypeptides) and are expected to serve as effective targets for cancer therapy in mammals.

Accordingly, in one embodiment of the present invention, the invention provides an isolated nucleic acid molecule having a nucleotide sequence that encodes a tumor antigen of hematopoietic origin polypeptide (a "TAHO" polypeptide) or fragment thereof.

In certain aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% nucleic acid sequence identity, to (a) a DNA molecule encoding a full-length TAHO polypeptide having an amino acid sequence as disclosed herein, a TAHO polypeptide amino

acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane TAHO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length TAHO polypeptide amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% nucleic acid sequence identity, to (a) a DNA molecule comprising the coding sequence of a full-length TAHO polypeptide cDNA as disclosed herein, the coding sequence of a TAHO polypeptide lacking the signal peptide as disclosed herein, the coding sequence of an extracellular domain of a transmembrane TAHO polypeptide, with or without the signal peptide, as disclosed herein or the coding sequence of any other specifically defined fragment of the full-length TAHO polypeptide amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In further aspects, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% nucleic acid sequence identity, to (a) a DNA molecule that encodes the same mature polypeptide encoded by the full-length coding region of any of the human protein cDNAs deposited with the ATCC as disclosed herein, or (b) the complement of the DNA molecule of (a).

Another aspect of the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a TAHO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide(s) are disclosed herein. Therefore, soluble extracellular domains of the herein described TAHO polypeptides are contemplated.

In other aspects, the present invention is directed to isolated nucleic acid molecules which hybridize to (a) a nucleotide sequence encoding a TAHO polypeptide having a full-length amino acid sequence as disclosed herein, a TAHO polypeptide amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane TAHO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length TAHO polypeptide amino acid sequence as disclosed herein, or (b) the complement of the nucleotide sequence of (a). In this regard, an embodiment of the present invention is directed to fragments of a full-length TAHO polypeptide coding sequence, or the complement thereof, as disclosed herein, that may find use as, for example, hybridization probes useful as, for example, detection probes, antisense oligonucleotide probes, or for encoding fragments of a full-length TAHO polypeptide that may optionally encode a polypeptide comprising a binding site for an anti-TAHO polypeptide antibody, a TAHO binding oligopeptide or other small organic molecule that binds to a TAHO polypeptide. Such nucleic acid fragments are usually at least about 5 nucleotides in length, alternatively at least about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360,

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370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 610, 620, 630, 640, 650, 660, 670, 680, 690, 700, 710, 720, 730, 740, 750, 760, 770, 780, 790, 800, 810, 820, 830, 840, 850, 860, 870, 880, 890, 900, 910, 920, 930, 940, 950, 960, 970, 980, 990, or 1000 nucleotides in length, wherein in this context the term “about” means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a TAHO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the TAHO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which TAHO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such novel fragments of TAHO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the TAHO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those TAHO polypeptide fragments that comprise a binding site for an anti-TAHO antibody, a TAHO binding oligopeptide or other small organic molecule that binds to a TAHO polypeptide.

In another embodiment, the invention provides isolated TAHO polypeptides encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a certain aspect, the invention concerns an isolated TAHO polypeptide, comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity, to a TAHO polypeptide having a full-length amino acid sequence as disclosed herein, a TAHO polypeptide amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane TAHO polypeptide protein, with or without the signal peptide, as disclosed herein, an amino acid sequence encoded by any of the nucleic acid sequences disclosed herein or any other specifically defined fragment of a full-length TAHO polypeptide amino acid sequence as disclosed herein.

In a further aspect, the invention concerns an isolated TAHO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% amino acid sequence identity, to an amino acid sequence encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein.

In a specific aspect, the invention provides an isolated TAHO polypeptide without the N-terminal signal sequence and/or without the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as hereinbefore described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the TAHO polypeptide and recovering the TAHO polypeptide from the cell culture.

Another aspect of the invention provides an isolated TAHO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid mol-

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ecule under conditions suitable for expression of the TAHO polypeptide and recovering the TAHO polypeptide from the cell culture.

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cells comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli* cells, or yeast cells. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides isolated chimeric polypeptides comprising any of the herein described TAHO polypeptides fused to a heterologous (non-TAHO) polypeptide. Example of such chimeric molecules comprise any of the herein described TAHO polypeptides fused to a heterologous polypeptide such as, for example, an epitope tag sequence or a Fc region of an immunoglobulin.

In another embodiment, the invention provides an antibody which binds, preferably specifically, to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, antibody fragment, chimeric antibody, humanized antibody, single-chain antibody or antibody that competitively inhibits the binding of an anti-TAHO polypeptide antibody to its respective antigenic epitope. Antibodies of the present invention may optionally be conjugated to a growth inhibitory agent or cytotoxic agent such as a toxin, including, for example, a maytansinoid or calicheamicin, an antibiotic, a radioactive isotope, a nucleolytic enzyme, or the like. The antibodies of the present invention may optionally be produced in CHO cells or bacterial cells and preferably induce death of a cell to which they bind. For detection purposes, the antibodies of the present invention may be detectably labeled, attached to a solid support, or the like.

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described antibodies. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli* cells, or yeast cells. A process for producing any of the herein described antibodies is further provided and comprises culturing host cells under conditions suitable for expression of the desired antibody and recovering the desired antibody from the cell culture.

In another embodiment, the invention provides oligopeptides (“TAHO binding oligopeptides”) which bind, preferably specifically, to any of the above or below described TAHO polypeptides. Optionally, the TAHO binding oligopeptides of the present invention may be conjugated to a growth inhibitory agent or cytotoxic agent such as a toxin, including, for example, a maytansinoid or calicheamicin, an antibiotic, a radioactive isotope, a nucleolytic enzyme, or the like. The TAHO binding oligopeptides of the present invention may optionally be produced in CHO cells or bacterial cells and preferably induce death of a cell to which they bind. For detection purposes, the TAHO binding oligopeptides of the present invention may be detectably labeled, attached to a solid support, or the like.

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described TAHO binding oligopeptides. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli* cells, or yeast cells. A process for producing any of the herein described TAHO binding oligopeptides is further provided and comprises culturing host cells under conditions suitable

for expression of the desired oligopeptide and recovering the desired oligopeptide from the cell culture.

In another embodiment, the invention provides small organic molecules ("TAHO binding organic molecules") which bind, preferably specifically, to any of the above or below described TAHO polypeptides. Optionally, the TAHO binding organic molecules of the present invention may be conjugated to a growth inhibitory agent or cytotoxic agent such as a toxin, including, for example, a maytansinoid or calicheamicin, an antibiotic, a radioactive isotope, a nucleolytic enzyme, or the like. The TAHO binding organic molecules of the present invention preferably induce death of a cell to which they bind. For detection purposes, the TAHO binding organic molecules of the present invention may be detectably labeled, attached to a solid support, or the like.

In a still further embodiment, the invention concerns a composition of matter comprising a TAHO polypeptide as described herein, a chimeric TAHO polypeptide as described herein, an anti-TAHO antibody as described herein, a TAHO binding oligopeptide as described herein, or a TAHO binding organic molecule as described herein, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

In yet another embodiment, the invention concerns an article of manufacture comprising a container and a composition of matter contained within the container, wherein the composition of matter may comprise a TAHO polypeptide as described herein, a chimeric TAHO polypeptide as described herein, an anti-TAHO antibody as described herein, a TAHO binding oligopeptide as described herein, or a TAHO binding organic molecule as described herein. The article may further optionally comprise a label affixed to the container, or a package insert included with the container, that refers to the use of the composition of matter for the therapeutic treatment.

Another embodiment of the present invention is directed to the use of a TAHO polypeptide as described herein, a chimeric TAHO polypeptide as described herein, an anti-TAHO polypeptide antibody as described herein, a TAHO binding oligopeptide as described herein, or a TAHO binding organic molecule as described herein, for the preparation of a medicament useful in the treatment of a condition which is responsive to the TAHO polypeptide, chimeric TAHO polypeptide, anti-TAHO polypeptide antibody, TAHO binding oligopeptide, or TAHO binding organic molecule.

B. Further Additional Embodiments

In yet further embodiments, the invention is directed to the following set of potential claims for this application:

1. Isolated nucleic acid having a nucleotide sequence that has at least 80% nucleic acid sequence identity to:

(a) a DNA molecule encoding the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO:

61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) a DNA molecule encoding the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26); FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) a DNA molecule encoding an extracellular domain of the polypeptide having the amino acid selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) a DNA molecule encoding an extracellular domain of the polypeptide having the amino acid selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ

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(SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70);

or

(g) the complement of (a), (b), (c), (d), (e) or (f).

3. Isolated nucleic acid that hybridizes to:

(a) a nucleic acid that encodes the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) a nucleic acid that encodes the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) a nucleic acid that encodes an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) a nucleic acid that encodes an extracellular domain of the polypeptide having the amino acid sequence selected

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from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70);

(f) the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70);

or

(g) the complement of (a), (b), (c), (d), (e) or (f).

4. The nucleic acid of Claim 3, wherein the hybridization occurs under stringent conditions.

5. The nucleic acid of Claim 3 which is at least about 5 nucleotides in length.

6. An expression vector comprising the nucleic acid of Claim 1, 2 or 3.

7. The expression vector of Claim 6, wherein said nucleic acid is operably linked to control sequences recognized by a host cell transformed with the vector.

8. A host cell comprising the expression vector of Claim 7.

9. The host cell of Claim 8 which is a CHO cell, an *E. coli* cell or a yeast cell.

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ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(c) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide sequence;

(d) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(e) an amino acid sequence encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56),

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FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) an amino acid sequence encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70).

13. A chimeric polypeptide comprising the polypeptide of Claim 11 or 12 fused to a heterologous polypeptide.

14. The chimeric polypeptide of Claim 13, wherein said heterologous polypeptide is an epitope tag sequence or an Fc region of an immunoglobulin.

15. An isolated antibody that binds to a polypeptide having at least 80% amino acid sequence identity to:

(a) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(e) an amino acid sequence encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) an amino acid sequence encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70).

17. The antibody of Claim 15 or 16 which is a monoclonal antibody.

18. The antibody of Claim 15 or 16 which is an antibody fragment.

19. The antibody of Claim 15 or 16 which is a chimeric or a humanized antibody.

20. The antibody of Claim 15 or 16 which is conjugated to a growth inhibitory agent.

21. The antibody of Claim 15 or 16 which is conjugated to a cytotoxic agent.

22. The antibody of Claim 21, wherein the cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

23. The antibody of Claim 21, wherein the cytotoxic agent is a toxin.

24. The antibody of Claim 23, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

25. The antibody of Claim 23, wherein the toxin is a maytansinoid.

26. The antibody of Claim 15 or 16 which is produced in bacteria.

27. The antibody of Claim 15 or 16 which is produced in CHO cells.

28. The antibody of Claim 15 or 16 which induces death of a cell to which it binds.

29. The antibody of Claim 15 or 16 which is detectably labeled.

30. An isolated nucleic acid having a nucleotide sequence that encodes the antibody of Claim 15 or 16.

31. An expression vector comprising the nucleic acid of Claim 30 operably linked to control sequences recognized by a host cell transformed with the vector.

32. A host cell comprising the expression vector of Claim 31.

33. The host cell of Claim 32 which is a CHO cell, an *E. coli* cell or a yeast cell.

34. A process for producing an antibody comprising culturing the host cell of Claim 32 under conditions suitable for expression of said antibody and recovering said antibody from the cell culture.

35. An isolated oligopeptide that binds to a polypeptide having at least 80% amino acid sequence identity to:

(a) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of

NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(e) an amino acid sequence encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) an amino acid sequence encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70).

37. The oligopeptide of Claim 35 or 36 which is conjugated to a growth inhibitory agent.

38. The oligopeptide of Claim 35 or 36 which is conjugated to a cytotoxic agent.

39. The oligopeptide of Claim 38, wherein the cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

40. The oligopeptide of Claim 38, wherein the cytotoxic agent is a toxin.

41. The oligopeptide of Claim 40, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

42. The oligopeptide of Claim 40, wherein the toxin is a maytansinoid.

43. The oligopeptide of Claim 35 or 36 which induces death of a cell to which it binds.

44. The oligopeptide of Claim 35 or 36 which is detectably labeled.

45. A TAHO binding organic molecule that binds to a polypeptide having at least 80% amino acid sequence identity to:

(a) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12),

FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) an amino acid sequence encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70).

47. The organic molecule of Claim 45 or 46 which is conjugated to a growth inhibitory agent.

48. The organic molecule of Claim 45 or 46 which is conjugated to a cytotoxic agent.

49. The organic molecule of Claim 48, wherein the cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

50. The organic molecule of Claim 48, wherein the cytotoxic agent is a toxin.

51. The organic molecule of Claim 50, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

52. The organic molecule of Claim 50, wherein the toxin is a maytansinoid.

53. The organic molecule of Claim 45 or 46 which induces death of a cell to which it binds.

54. The organic molecule of Claim 45 or 46 which is detectably labeled.

55. A composition of matter comprising:

- (a) the polypeptide of Claim 11;
- (b) the polypeptide of Claim 12;
- (c) the antibody of Claim 15;
- (d) the antibody of Claim 16;
- (e) the oligopeptide of Claim 35;
- (f) the oligopeptide of Claim 36;
- (g) the TAHO binding organic molecule of Claim 45; or
- (h) the TAHO binding organic molecule of Claim 46; in combination with a carrier.

56. The composition of matter of Claim 55, wherein said carrier is a pharmaceutically acceptable carrier.

57. An article of manufacture comprising:

- (a) a container; and
- (b) the composition of matter of Claim 55 contained within said container.

58. The article of manufacture of Claim 57 further comprising a label affixed to said container, or a package insert included

with said container, referring to the use of said composition of matter for the therapeutic treatment of or the diagnostic detection of a cancer.

59. A method of inhibiting the growth of a cell that expresses a protein having at least 80% amino acid sequence identity to:

(a) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22

(SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) a polypeptide encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) a polypeptide encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70), said method comprising contacting said cell with an antibody, oligopeptide or organic molecule that binds to said protein, the binding of said antibody, oligopeptide or organic molecule to said protein thereby causing an inhibition of growth of said cell.

60. The method of Claim 59, wherein said antibody is a monoclonal antibody.

61. The method of Claim 59, wherein said antibody is an antibody fragment.

62. The method of Claim 59, wherein said antibody is a chimeric or a humanized antibody.

63. The method of Claim 59, wherein said antibody, oligopeptide or organic molecule is conjugated to a growth inhibitory agent.

64. The method of Claim 59, wherein said antibody, oligopeptide or organic molecule is conjugated to a cytotoxic agent.

65. The method of Claim 64, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

66. The method of Claim 64, wherein the cytotoxic agent is a toxin.

67. The method of Claim 66, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

68. The method of Claim 66, wherein the toxin is a maytansinoid.

69. The method of Claim 59, wherein said antibody is produced in bacteria.

70. The method of Claim 59, wherein said antibody is produced in CHO cells.

71. The method of Claim 59, wherein said cell is a hematopoietic cell.

72. The method of Claim 71, wherein said hematopoietic cell is selected from the group consisting of a lymphocyte, leukocyte, platelet, erythrocyte and natural killer cell.

73. The method of Claim 72, wherein said lymphocyte is a B cell or T cell.

74. The method of claim 73 wherein said lymphocyte is a cancer cell.

75. The method of claim 74 wherein said cancer cell is further exposed to radiation treatment or a chemotherapeutic agent.

76. The method of claim 75, wherein said cancer cell is selected from the group consisting of a lymphoma cell, a myeloma cell and a leukemia cell.

77. The method of Claim 71, wherein said protein is more abundantly expressed by said hematopoietic cell as compared to a non-hematopoietic cell.

78. The method of Claim 59 which causes the death of said cell.

79. The method of Claim 59, wherein said protein has:

(a) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ

ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) a polypeptide encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70);

or

(f) a polypeptide encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70), said method comprising administering to said mammal a therapeutically effective amount of an antibody, oligopeptide or organic molecule that binds to said protein, thereby effectively treating said mammal.

81. The method of Claim 80, wherein said antibody is a monoclonal antibody.

82. The method of Claim 80, wherein said antibody is an antibody fragment.

83. The method of Claim 80, wherein said antibody is a chimeric or a humanized antibody.

84. The method of Claim 80, wherein said antibody, oligopeptide or organic molecule is conjugated to a growth inhibitory agent.

85. The method of Claim 80, wherein said antibody, oligopeptide or organic molecule is conjugated to a cytotoxic agent.

86. The method of Claim 85, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

87. The method of Claim 85, wherein the cytotoxic agent is a toxin.

88. The method of Claim 87, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

89. The method of Claim 87, wherein the toxin is a maytansinoid.

90. The method of Claim 80, wherein said antibody is produced in bacteria.

91. The method of Claim 80, wherein said antibody is produced in CHO cells.

92. The method of Claim 80, wherein said tumor is further exposed to radiation treatment or a chemotherapeutic agent.

93. The method of Claim 80, wherein said tumor is a lymphoma, leukemia or myeloma tumor.

94. The method of Claim 80, wherein said protein is more abundantly expressed by a hematopoietic cell as compared to a non-hematopoietic cell of said tumor.

95. The method of Claim 94, wherein said protein is more abundantly expressed by cancerous hematopoietic cells of said tumor as compared to normal hematopoietic cells of said tumor.

96. The method of Claim 80, wherein said protein has:

(a) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ

ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) a polypeptide encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) a polypeptide encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70), said method comprising exposing said sample to an antibody, oligopeptide or organic molecule that binds to said protein and determining binding of said antibody, oligopeptide or organic molecule to said protein in said sample, wherein binding of the antibody, oligopeptide or organic molecule to said protein is indicative of the presence of said protein in said sample.

98. The method of Claim 97, wherein said sample comprises a cell suspected of expressing said protein.

99. The method of Claim 98, wherein said cell is a cancer cell.

100. The method of Claim 97, wherein said antibody, oligopeptide or organic molecule is detectably labeled.

101. The method of Claim 97, wherein said protein has:

(a) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(c) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide sequence;

(d) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide sequence;

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(SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) a polypeptide encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70), said method comprising administering to a subject in need of such treatment an effective amount of an antagonist of said protein, thereby effectively treating or preventing said cell proliferative disorder.

103. The method of Claim 102, wherein said cell proliferative disorder is cancer.

104. The method of Claim 102, wherein said antagonist is an anti-TAHO polypeptide antibody, TAHO binding oligopeptide, TAHO binding organic molecule or antisense oligonucleotide.

105. A method of binding an antibody, oligopeptide or organic molecule to a cell that expresses a protein having at least 80% amino acid sequence identity to:

(a) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ

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ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) a polypeptide encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ

ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) a polypeptide encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 56, FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70), said method comprising contacting said cell with an antibody, oligopeptide or organic molecule that binds to said protein and allowing the binding of the antibody, oligopeptide or organic molecule to said protein to occur, thereby binding said antibody, oligopeptide or organic molecule to said cell.

106. The method of Claim 105, wherein said antibody is a monoclonal antibody.

107. The method of Claim 105, wherein said antibody is an antibody fragment.

108. The method of Claim 105, wherein said antibody is a chimeric or a humanized antibody.

109. The method of Claim 105, wherein said antibody, oligopeptide or organic molecule is conjugated to a growth inhibitory agent.

110. The method of Claim 105, wherein said antibody, oligopeptide or organic molecule is conjugated to a cytotoxic agent.

111. The method of Claim 110, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

112. The method of Claim 110, wherein the cytotoxic agent is a toxin.

113. The method of Claim 112, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

114. The method of Claim 112, wherein the toxin is a maytansinoid.

115. The method of Claim 105, wherein said antibody is produced in bacteria.

116. The method of Claim 105, wherein said antibody is produced in CHO cells.

117. The method of Claim 105, wherein said cell is a hematopoietic cell.

118. The method of Claim 117, wherein said hematopoietic cell is selected from the group consisting of a lymphocyte, leukocyte, platelet, erythrocyte and natural killer cell.

119. The method of claim 118, wherein said lymphocyte is a B cell or a T cell.

120. The method of Claim 119, wherein said lymphocyte is a cancer cell.

121. The method of Claim 120 wherein said cancer cell is further exposed to radiation treatment or a chemotherapeutic agent.

122. The method of Claim 120, wherein said cancer cell is selected from the group consisting of a leukemia cell, a lymphoma cell and a myeloma cell.

123. The method of Claim 120, wherein said protein is more abundantly expressed by said hematopoietic cell as compared to a non-hematopoietic cell.

124. The method of Claim 105 which causes the death of said cell.

125. Use of a nucleic acid as claimed in any of Claims 1 to 5 or 30 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

126. Use of a nucleic acid as claimed in any of Claims 1 to 5 or 30 in the preparation of a medicament for treating a tumor.

127. Use of a nucleic acid as claimed in any of Claims 1 to 5 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

128. Use of an expression vector as claimed in Claim 6 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

129. Use of an expression vector as claimed in Claim 6 in the preparation of medicament for treating a tumor.

130. Use of an expression vector as claimed in Claim 6 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

131. Use of a host cell as claimed in Claim 8 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

132. Use of a host cell as claimed in Claim 8 in the preparation of a medicament for treating a tumor.

133. Use of a host cell as claimed in Claim 8 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

134. Use of a polypeptide as claimed in Claim 11 or 12 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

135. Use of a polypeptide as claimed in Claim 11 or 12 in the preparation of a medicament for treating a tumor.

136. Use of a polypeptide as claimed in Claim 11 or 12 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

137. Use of an antibody as claimed in Claim 15 or 16 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

138. Use of an antibody as claimed in Claim 15 or 16 in the preparation of a medicament for treating a tumor.

139. Use of an antibody as claimed in Claim 15 or 16 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

140. Use of an oligopeptide as claimed in Claim 35 or 36 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

141. Use of an oligopeptide as claimed in Claim 35 or 36 in the preparation of a medicament for treating a tumor.

142. Use of an oligopeptide as claimed in Claim 35 or 36 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

143. Use of a TAHO binding organic molecule as claimed in Claim 45 or 46 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

144. Use of a TAHO binding organic molecule as claimed in Claim 45 or 46 in the preparation of a medicament for treating a tumor.

145. Use of a TAHO binding organic molecule as claimed in Claims 45 or 46 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

146. Use of a composition of matter as claimed in Claim 55 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

147. Use of a composition of matter as claimed in Claim 55 in the preparation of a medicament for treating a tumor.

148. Use of a composition of matter as claimed in Claim 55 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

149. Use of an article of manufacture as claimed in Claim 57 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

150. Use of an article of manufacture as claimed in Claim 58 in the preparation of a medicament for treating a tumor.

151. Use of an article of manufacture as claimed in Claim 58 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

152. A method for inhibiting the growth of a cell, wherein the growth of said cell is at least in part dependent upon a growth potentiating effect of a protein having at least 80% amino acid sequence identity to:

(a) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71),

(b) the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(c) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42

(SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide;

(d) an extracellular domain of the polypeptide having the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide;

(e) a polypeptide encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) a polypeptide encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70), said method comprising contacting said

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protein with an antibody, oligopeptide or organic molecule that binds to said protein, there by inhibiting the growth of said cell.

153. The method of Claim 152, wherein said cell is a hematopoietic cell.

154. The method of Claim 152, wherein said protein is expressed by said cell.

155. The method of Claim 152, wherein the binding of said antibody, oligopeptide or organic molecule to said protein antagonizes a cell growth-potentiating activity of said protein.

156. The method of Claim 152, wherein the binding of said antibody, oligopeptide or organic molecule to said protein induces the death of said cell.

157. The method of Claim 152, wherein said antibody is a monoclonal antibody.

158. The method of Claim 152, wherein said antibody is an antibody fragment.

159. The method of Claim 152, wherein said antibody is a chimeric or a humanized antibody.

160. The method of Claim 152, wherein said antibody, oligopeptide or organic molecule is conjugated to a growth inhibitory agent.

161. The method of Claim 152, wherein said antibody, oligopeptide or organic molecule is conjugated to a cytotoxic agent.

162. The method of Claim 161, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

163. The method of Claim 161, wherein the cytotoxic agent is a toxin.

164. The method of Claim 163, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

165. The method of Claim 163, wherein the toxin is a maytansinoid.

166. The method of Claim 152, wherein said antibody is produced in bacteria.

167. The method of Claim 152, wherein said antibody is produced in CHO cells.

168. The method of Claim 152, wherein said protein has:

(a) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO:

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34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(c) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide sequence;

(d) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(e) an amino acid sequence encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

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70 (SEQ ID NO: 70), said method comprising contacting said protein with an antibody, oligopeptide or organic molecule that binds to said protein, thereby effectively treating said tumor.

170. The method of Claim 169, wherein said protein is expressed by cells of said tumor.

171. The method of Claim 169, wherein the binding of said antibody, oligopeptide or organic molecule to said protein antagonizes a cell growth-potentiating activity of said protein.

172. The method of Claim 169, wherein said antibody is a monoclonal antibody.

173. The method of Claim 169, wherein said antibody is an antibody fragment.

174. The method of Claim 169, wherein said antibody is a chimeric or a humanized antibody.

175. The method of Claim 169, wherein said antibody, oligopeptide or organic molecule is conjugated to a growth inhibitory agent.

176. The method of Claim 169, wherein said antibody, oligopeptide or organic molecule is conjugated to a cytotoxic agent.

177. The method of Claim 176, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

178. The method of Claim 176, wherein the cytotoxic agent is a toxin.

179. The method of Claim 178, wherein the toxin is selected from the group consisting of maytansinoid and calicheamicin.

180. The method of Claim 178, wherein the toxin is a maytansinoid.

181. The method of Claim 169, wherein said antibody is produced in bacteria.

182. The method of Claim 169, wherein said antibody is produced in CHO cells.

183. The method of Claim 169, wherein said protein has:

(a) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71);

(b) the amino acid sequence selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO:

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55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(c) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), with its associated signal peptide sequence;

(d) an amino acid sequence of an extracellular domain of the polypeptide selected from the group consisting of the amino acid sequence shown in FIG. 2 (SEQ ID NO: 2), FIG. 4 (SEQ ID NO: 4), FIG. 6 (SEQ ID NO: 6), FIG. 8 (SEQ ID NO: 8), FIG. 10 (SEQ ID NO: 10), FIG. 12 (SEQ ID NO: 12), FIG. 14 (SEQ ID NO: 14), FIG. 16 (SEQ ID NO: 16), FIG. 18 (SEQ ID NO: 18), FIG. 20 (SEQ ID NO: 20), FIG. 22 (SEQ ID NO: 22), FIG. 24 (SEQ ID NO: 24), FIG. 26 (SEQ ID NO: 26), FIG. 28 (SEQ ID NO: 28), FIG. 30 (SEQ ID NO: 30), FIG. 32 (SEQ ID NO: 32), FIG. 34 (SEQ ID NO: 34), FIG. 36 (SEQ ID NO: 36), FIG. 40 (SEQ ID NO: 40), FIG. 42 (SEQ ID NO: 42), FIG. 44 (SEQ ID NO: 44), FIG. 46 (SEQ ID NO: 46), FIG. 49 (SEQ ID NO: 49), FIG. 51 (SEQ ID NO: 51), FIG. 53 (SEQ ID NO: 53), FIG. 55 (SEQ ID NO: 55), FIG. 57 (SEQ ID NO: 57), FIG. 59 (SEQ ID NO: 59), FIG. 61 (SEQ ID NO: 61), FIG. 63 (SEQ ID NO: 63), FIG. 65 (SEQ ID NO: 65), FIG. 67 (SEQ ID NO: 67), FIG. 69 (SEQ ID NO: 69) and FIG. 71 (SEQ ID NO: 71), lacking its associated signal peptide sequence;

(e) an amino acid sequence encoded by the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11 (SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70); or

(f) an amino acid sequence encoded by the full-length coding region of the nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIG. 1 (SEQ ID NO: 1), FIG. 3 (SEQ ID NO: 3), FIG. 5 (SEQ ID NO: 5), FIG. 7 (SEQ ID NO: 7), FIG. 9 (SEQ ID NO: 9), FIG. 11

(SEQ ID NO: 11), FIG. 13 (SEQ ID NO: 13), FIG. 15 (SEQ ID NO: 15), FIG. 17 (SEQ ID NO: 17), FIG. 19 (SEQ ID NO: 19), FIG. 21 (SEQ ID NO: 21), FIG. 23 (SEQ ID NO: 23), FIG. 25 (SEQ ID NO: 25), FIG. 27 (SEQ ID NO: 27), FIG. 29 (SEQ ID NO: 29), FIG. 31 (SEQ ID NO: 31), FIG. 33 (SEQ ID NO: 33), FIG. 35 (SEQ ID NO: 35), FIG. 37 (SEQ ID NO: 37), FIG. 39 (SEQ ID NO: 39), FIG. 41 (SEQ ID NO: 41), FIG. 43 (SEQ ID NO: 43), FIG. 45 (SEQ ID NO: 45), FIG. 47 (SEQ ID NO: 47), FIG. 48 (SEQ ID NO: 48), FIG. 50 (SEQ ID NO: 50), FIG. 52 (SEQ ID NO: 52), FIG. 54 (SEQ ID NO: 54), FIG. 56 (SEQ ID NO: 56), FIG. 58 (SEQ ID NO: 58), FIG. 60 (SEQ ID NO: 60), FIG. 62 (SEQ ID NO: 62), FIG. 64 (SEQ ID NO: 64), FIG. 66 (SEQ ID NO: 66), FIG. 68 (SEQ ID NO: 68) and FIG. 70 (SEQ ID NO: 70).

184. A composition of matter comprising the chimeric polypeptide of Claim 13.

185. Use of a nucleic acid as claimed in Claim 30 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

186. Use of an expression vector as claimed in Claim 7 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

187. Use of an expression vector as claimed in Claim 31 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

188. Use of an expression vector as claimed in Claim 7 in the preparation of medicament for treating a tumor.

189. Use of an expression vector as claimed in Claim 31 in the preparation of medicament for treating a tumor.

190. Use of an expression vector as claimed in Claim 7 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

191. Use of an expression vector as claimed in Claim 31 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

192. Use of a host cell as claimed in Claim 9 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

193. Use of a host cell as claimed in Claim 32 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

194. Use of a host cell as claimed in Claim 33 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

195. Use of a host cell as claimed in Claim 9 in the preparation of a medicament for treating a tumor.

196. Use of a host-cell as claimed in Claim 32 in the preparation of a medicament for treating a tumor.

197. Use of a host cell as claimed in Claim 33 in the preparation of a medicament for treating a tumor.

198. Use of a host cell as claimed in Claim 9 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

199. Use of a host cell as claimed in Claim 32 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

200. Use of a host cell as claimed in Claim 33 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

201. Use of a polypeptide as claimed in Claim 13 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

202. Use of a polypeptide as claimed in Claim 14 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

203. Use of a polypeptide as claimed in Claim 13 in the preparation of a medicament for treating a tumor.

204. Use of a polypeptide as claimed in Claim 14 in the preparation of a medicament for treating at tumor.

205. Use of a polypeptide as claimed in Claim 13 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

206. Use of a polypeptide as claimed in Claim 14 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

207. Use of an antibody as claimed in Claim 17 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

208. Use of an antibody as claimed in Claim 18 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

209. Use of an antibody as claimed in Claim 19 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

210. Use of an antibody as claimed in Claim 20 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

211. Use of an antibody as claimed in Claim 21 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

212. Use of an antibody as claimed in Claim 22 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

213. Use of an antibody as claimed in Claim 23 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

214. Use of an antibody as claimed in Claim 24 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

215. Use of an antibody as claimed in Claim 25 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

216. Use of an antibody as claimed in Claim 26 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

217. Use of an antibody as claimed in Claim 27 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

218. Use of an antibody as claimed in Claim 28 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

219. Use of an antibody as claimed in Claim 29 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

220. Use of an antibody as claimed in Claim 17 in the preparation of a medicament for treating a tumor.

221. Use of an antibody as claimed in Claim 18 in the preparation of a medicament for treating a tumor.

222. Use of an antibody as claimed in Claim 19 in the preparation of a medicament for treating a tumor.

223. Use of an antibody as claimed in Claim 20 in the preparation of a medicament for treating a tumor.

224. Use of an antibody as claimed in Claim 21 in the preparation of a medicament for treating a tumor.

225. Use of an antibody as claimed in Claim 22 in the preparation of a medicament for treating a tumor.

226. Use of an antibody as claimed in Claim 23 in the preparation of a medicament for treating a tumor.

227. Use of an antibody as claimed in Claim 24 in the preparation of a medicament for treating a tumor.

228. Use of an antibody as claimed in Claim 25 in the preparation of a medicament for treating a tumor.

229. Use of an antibody as claimed in Claim 26 in the preparation of a medicament for treating a tumor.

278. Use of a TAHO binding organic molecule as claimed in Claim 53 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

279. Use of a TAHO binding organic molecule as claimed in Claim 54 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

280. Use of a TAHO binding organic molecule as claimed in Claim 47 in the preparation of a medicament for treating a tumor.

281. Use of a TAHO binding organic molecule as claimed in Claim 48 in the preparation of a medicament for treating a tumor.

282. Use of a TAHO binding organic molecule as claimed in Claim 49 in the preparation of a medicament for treating a tumor.

283. Use of a TAHO binding organic molecule as claimed in Claim 50 in the preparation of a medicament for treating a tumor.

284. Use of a TAHO binding organic molecule as claimed in Claim 51 in the preparation of a medicament for treating a tumor.

285. Use of a TAHO binding organic molecule as claimed in Claim 52 in the preparation of a medicament for treating a tumor.

286. Use of a TAHO binding organic molecule as claimed in Claim 53 in the preparation of a medicament for treating a tumor.

287. Use of a TAHO binding organic molecule as claimed in Claim 54 in the preparation of a medicament for treating a tumor.

288. Use of a TAHO binding organic molecule as claimed in Claim 47 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

289. Use of a TAHO binding organic molecule as claimed in Claim 48 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

290. Use of a TAHO binding organic molecule as claimed in Claim 49 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

291. Use of a TAHO binding organic molecule as claimed in Claim 50 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

292. Use of a TAHO binding organic molecule as claimed in Claim 51 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

293. Use of a TAHO binding organic molecule as claimed in Claim 52 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

294. Use of a TAHO binding organic molecule as claimed in Claim 53 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

295. Use of a TAHO binding organic molecule as claimed in Claim 54 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

296. Use of a composition of matter as claimed in Claim 56 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

297. Use of a composition of matter as claimed in Claim 56 in the preparation of a medicament for treating a tumor.

298. Use of a composition of matter as claimed in Claim 56 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

299. Use of an article of manufacture as claimed in Claim 58 in the preparation of a medicament for the therapeutic treatment or diagnostic detection of a cancer.

300. Use of an article of manufacture as claimed in Claim 58 in the preparation of a medicament for treating a tumor.

301. Use of an article of manufacture as claimed in Claim 58 in the preparation of a medicament for treatment or prevention of a cell proliferative disorder.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a nucleotide sequence (SEQ ID NO: 1) of a TAHO1 (PRO7201) cDNA, wherein SEQ ID NO: 1 is a clone designated herein as "DNA105250" (also referred here in as "CD180" or "LY64").

FIG. 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in FIG. 1.

FIG. 3 shows a nucleotide sequence (SEQ ID NO:3) of a TAHO2 (PRO4644) cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA150004" (also referred here in as "CD20" or "MSA41").

FIG. 4 shows the amino acid sequence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in FIG. 3.

FIG. 5 shows a nucleotide sequence (SEQ ID NO:5) of a TAHO3 (PRO31998) cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA182432" (also referred here in as "FcRH2" or "SPAP1").

FIG. 6 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in FIG. 5.

FIG. 7 shows a nucleotide sequence (SEQ ID NO:7) of a TAHO4 (PRO36248) cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA225785" (also referred here in as "CD79A").

FIG. 8 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in FIG. 7.

FIG. 9 shows a nucleotide sequence (SEQ ID NO:9) of a TAHO5 (PRO36249) cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA225786" (also referred here in as "CD79B").

FIG. 10 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in FIG. 9.

FIG. 11 shows a nucleotide sequence (SEQ ID NO:11) of a TAHO6 (PRO36338) wherein SEQ ID NO:11 is a clone designated herein as "DNA225875" (also referred here in as "CD21" or "CR2").

FIG. 12 shows the amino acid sequence (SEQ ID NO: 12) derived from the coding sequence of SEQ ID NO:11 shown in FIG. 11.

FIG. 13 shows a nucleotide sequence (SEQ ID NO:13) of a TAHO7 (PRO36642) wherein SEQ ID NO: 13 is a clone designated herein as "DNA226179" (also referred here in as "CCR6").

FIG. 14 shows the amino acid sequence (SEQ ID NO:14) derived from the coding sequence of SEQ ID NO: 13 shown in FIG. 13.

FIG. 15 shows a nucleotide sequence (SEQ ID NO: 15) of a TAHO8 (PRO36702) cDNA, wherein SEQ ID NO:15 is a clone designated herein as "DNA226239" (also referred here in as "CD72").

FIG. 16 shows the amino acid sequence (SEQ ID NO:16) derived from the coding sequence of SEQ ID NO:15 shown in FIG. 15.

FIG. 17 shows a nucleotide sequence (SEQ ID NO: 17) of a TAHO9 (PRO36857) cDNA, wherein SEQ ID NO:17 is a clone designated herein as "DNA226394" (also referred here in as "P2RX5").

FIG. 18 shows the amino acid sequence (SEQ ID NO: 18) derived from the coding sequence of SEQ ID NO: 17 shown in FIG. 17.

FIG. 19 shows a nucleotide sequence (SEQ ID NO: 19) of a TAHO10 (PRO36886) cDNA, wherein SEQ ID NO: 19 is a clone designated herein as "DNA226423" (also referred herein as "HLA-DOB").

FIG. 20 shows the amino acid sequence (SEQ ID NO:20) derived from the coding sequence of SEQ ID NO:19 shown in FIG. 19.

FIG. 21 shows a nucleotide sequence (SEQ ID NO:21) of a TAHO1 (PRO38244) cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA227781" (also referred herein as "CXCR5").

FIG. 22 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in FIG. 21.

FIG. 23 shows a nucleotide sequence (SEQ ID NO:23) of a TAHO12 (PRO38342) cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA227879" (also referred herein as "CD23" or "FCER2").

FIG. 24 shows the amino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in FIG. 23.

FIG. 25 shows a nucleotide sequence (SEQ ID NO:25) of a TAHO13 (PRO51405) cDNA, wherein SEQ ID NO:25 is a clone designated herein as "DNA256363" (also referred herein as "GPR2").

FIG. 26 shows the amino acid sequence (SEQ ID NO:26) derived from the coding sequence of SEQ ID NO:25 shown in FIG. 25.

FIG. 27 shows a nucleotide sequence (SEQ ID NO:27) of a TAHO14 (PRO87299) cDNA, wherein SEQ ID NO:27 is a clone designated herein as "DNA332467" (also referred herein as "Btig").

FIG. 28 shows the amino acid sequence (SEQ ID NO:28) derived from the coding sequence of SEQ ID NO:27 shown in FIG. 27.

FIG. 29 shows a nucleotide sequence (SEQ ID NO:29) of a TAHO15 (PRO1111) cDNA, wherein SEQ ID NO:29 is a clone designated herein as "DNA58721" (also referred herein as "NAG14").

FIG. 30 shows the amino acid sequence (SEQ ID NO:30) derived from the coding sequence of SEQ ID NO:29 shown in FIG. 29.

FIG. 31 shows a nucleotide sequence (SEQ ID NO:31) of a TAHO16 (PRO90213) cDNA, wherein SEQ ID NO:31 is a clone designated herein as "DNA335924" (also referred herein as "SLGC16270").

FIG. 32 shows the amino acid sequence (SEQ ID NO:32) derived from the coding sequence of SEQ ID NO:31 shown in FIG. 31.

FIG. 33 shows a nucleotide sequence (SEQ ID NO:33) of a TAHO17 (PRO85143) cDNA, wherein SEQ ID NO:33 is a clone designated herein as "DNA340394" (also referred herein as "FcRH1" or "IRTA5").

FIG. 34 shows the amino acid sequence (SEQ ID NO:34) derived from the coding sequence of SEQ ID NO:33 shown in FIG. 33.

FIG. 35 shows a nucleotide sequence (SEQ ID NO:35) of a TAHO18 (PRO820) cDNA, wherein SEQ ID NO:35 is a clone designated herein as "DNA56041" (also referred herein as "FcRH5" or "IRTA2").

FIG. 36 shows the amino acid sequence (SEQ ID NO:36) derived from the coding sequence of SEQ ID NO:35 shown in FIG. 35.

FIG. 37 shows a nucleotide sequence (SEQ ID NO:37) of a TAHO19 (PRO1140) cDNA, wherein SEQ ID NO:37 is a clone designated herein as "DNA59607" (also referred herein as "ATWD578").

FIG. 38 shows the amino acid sequence (SEQ ID NO:38) derived from the coding sequence of SEQ ID NO:37 shown in FIG. 37.

FIG. 39 shows a nucleotide sequence (SEQ ID NO:39) of a TAHO20 (PRO52483) cDNA, wherein SEQ ID NO:39 is a clone designated herein as "DNA257955" (also referred herein as "FcRH3" or "IRTA3").

FIG. 40 shows the amino acid sequence (SEQ ID NO:40) derived from the coding sequence of SEQ ID NO:39 shown in FIG. 39.

FIG. 41 shows a nucleotide sequence (SEQ ID NO:41) of a TAHO21 (PRO85193) cDNA, wherein SEQ ID NO:41 is a clone designated herein as "DNA329863" (also referred herein as "FcRH4" or "IRTA1").

FIG. 42 shows the amino acid sequence (SEQ ID NO:42) derived from the coding sequence of SEQ ID NO:41 shown in FIG. 41.

FIG. 43 shows a nucleotide sequence (SEQ ID NO:43) of a TAHO22 (PRO96849) cDNA, wherein SEQ ID NO:43 is a clone designated herein as "DNA346528" (also referred herein as "FcRH6" or "FAIL").

FIG. 44 shows the amino acid sequence (SEQ ID NO:44) derived from the coding sequence of SEQ ID NO:43 shown in FIG. 43.

FIG. 45 shows a nucleotide sequence (SEQ ID NO:45) of a TAHO23 (PRO34414) cDNA, wherein SEQ ID NO:45 is a clone designated herein as "DNA212930" (also referred herein as "BCMA").

FIG. 46 shows the amino acid sequence (SEQ ID NO:46) derived from the coding sequence of SEQ ID NO:45 shown in FIG. 45.

FIG. 47 shows a nucleotide sequence (SEQ ID NO:47) of a TAHO24 (PRO90207) cDNA, wherein SEQ ID NO:47 is a clone designated herein as "DNA335918" (also referred herein as "239287_at").

FIG. 48 shows a nucleotide sequence (SEQ ID NO: 48) of a TAHO25 (PRO36283) cDNA, wherein SEQ ID NO: 48 is a clone designated herein as "DNA225820" (also referred here in as "CD19").

FIG. 49 shows the amino acid sequence (SEQ ID NO: 49) derived from the coding sequence of SEQ ID NO: 48 shown in FIG. 48.

FIG. 50 shows a nucleotide sequence (SEQ ID NO: 50) of a TAHO26 (PRO2177) cDNA, wherein SEQ ID NO: 50 is a clone designated herein as "DNA88116" (also referred here in as "CD22").

FIG. 51 shows the amino acid sequence (SEQ ID NO: 51) derived from the coding sequence of SEQ ID NO: 50 shown in FIG. 50.

FIG. 52 shows a nucleotide sequence (SEQ ID NO: 52) of a TAHO27 (PRO38215) cDNA, wherein SEQ ID NO: 52 is a clone designated herein as "DNA227752" (also referred here in as "CXCR3").

FIG. 53 shows the amino acid sequence (SEQ ID NO: 53) derived from the coding sequence of SEQ ID NO: 52 shown in FIG. 52.

FIG. 54 shows a nucleotide sequence (SEQ ID NO: 54) of a TAHO28 (PRO9993) cDNA, wherein SEQ ID NO: 54 is a clone designated herein as "DNA119476" (also referred here in as "SILV").

FIG. 55 shows the amino acid sequence (SEQ ID NO: 55) derived from the coding sequence of SEQ ID NO: 54 shown in FIG. 54.

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FIG. 56 shows a nucleotide sequence (SEQ ID NO: 56) of a TAHO29 (PRO49980) cDNA, wherein SEQ ID NO: 56 is a cloned designated herein as "DNA254890" (also referred here in as "KCNK4").

FIG. 57 shows the amino acid sequence (SEQ ID NO: 57) derived from the coding sequence of SEQ ID NO: 56 shown in FIG. 56.

FIG. 58 shows a nucleotide sequence (SEQ ID NO: 58) of a TAHO30 (PRO34756) cDNA, wherein SEQ ID NO: 58 is a cloned designated herein as "DNA254890" (also referred here in as "CXorf1").

FIG. 59 shows the amino acid sequence (SEQ ID NO: 59) derived from the coding sequence of SEQ ID NO: 58 shown in FIG. 58.

FIG. 60 shows a nucleotide sequence (SEQ ID NO: 60) of a TAHO31 (PRO293) cDNA, wherein SEQ ID NO: 60 is a cloned designated herein as "DNA254890" (also referred here in as "LRRN5").

FIG. 61 shows the amino acid sequence (SEQ ID NO: 61) derived from the coding sequence of SEQ ID NO: 60 shown in FIG. 60.

FIG. 62 shows a nucleotide sequence (SEQ ID NO: 62) of a TAHO32 (PRO33767) cDNA, wherein SEQ ID NO: 62 is a cloned designated herein as "DNA210233".

FIG. 63 shows the amino acid sequence (SEQ ID NO: 63) derived from the coding sequence of SEQ ID NO: 62 shown in FIG. 62.

FIG. 64 shows a nucleotide sequence (SEQ ID NO: 64) of a TAHO33 (PRO258) cDNA, wherein SEQ ID NO: 64 is a cloned designated herein as "DNA35918" (also referred herein as "IGSF4B").

FIG. 65 shows the amino acid sequence (SEQ ID NO: 65) derived from the coding sequence of SEQ ID NO: 64 shown in FIG. 64.

FIG. 66 shows a nucleotide sequence (SEQ ID NO: 66) of a TAHO34 (PRO53968) cDNA, wherein SEQ ID NO: 66 is a cloned designated herein as "DNA260038".

FIG. 67 shows the amino acid sequence (SEQ ID NO: 67) derived from the coding sequence of SEQ ID NO: 66 shown in FIG. 66.

FIG. 68 shows a nucleotide sequence (SEQ ID NO: 68) of a TAHO35 (PRO89267) cDNA, wherein SEQ ID NO: 68 is a cloned designated herein as "DNA334818" (also referred herein as "FLJ12681").

FIG. 69 shows the amino acid sequence (SEQ ID NO: 69) derived from the coding sequence of SEQ ID NO: 68 shown in FIG. 68.

FIG. 70 shows a nucleotide sequence (SEQ ID NO: 70) of a TAHO36 (PRO51405) cDNA, wherein SEQ ID NO: 70 is a cloned designated herein as "DNA257501".

FIG. 71 shows the amino acid sequence (SEQ ID NO: 71) derived from the coding sequence of SEQ ID NO: 70 shown in FIG. 70.

FIG. 72 summarizes the Agilent human microarrays that demonstrate significant expression of TAHO15 in bone marrow plasma cells and multiple myeloma cells as compared to low expression in non-B cells, such as neutrophils, T cells and natural killer (NK) cells. TAHO15 is also significantly expressed in some non-hodgkin lymphoma cells.

FIGS. 73A-73D show microarray data showing the expression of TAHO1 in normal samples and in diseased samples, such as significant expression in Non-Hodgkin's Lymphoma (NHL) samples and normal B cells (NB). Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver),

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smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 74A-74D show microarray data showing the expression of TAHO2 in normal samples and in diseased samples, such as significant expression in NHL samples, follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB). Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 75A-75D show microarray data showing the expression of TAHO3 in normal samples and in diseased samples, such as significant expression in NHL samples, follicular lymphoma (FL) and memory B cells (mem B). Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 76A-76D show microarray data showing the expression of TAHO4 in normal samples and in diseased samples, such as significant expression in NHL samples and multiple myeloma samples (MM), and normal cerebellum and normal blood. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 77A-77D show microarray data showing the expression of TAHO5 in normal samples and in diseased samples, such as significant expression in NHL samples. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 78A-78D show microarray data showing the expression of TAHO6 in normal samples and in diseased samples, such as significant expression in NHL samples and normal lymph node (NLN). Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 79A-79D show microarray data showing the expression of TAHO8 in normal samples and in diseased samples, such as significant expression in NHL samples, multiple myeloma samples (MM), follicular lymphoma (FL) and normal tonsil. Abbreviations used in the Figures are designated

as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 80A-80B show microarray data showing the expression of TAHO9 in normal samples and in diseased samples, such as significant expression in normal B cells (circulating and lymph-node derived B cells) and not significantly expressed in non B cells and significantly expressed in normal plasma cells and multiple myeloma samples and the lymphoid organs, spleen and thymus. FIG. 80 is shown as two panels. The panel in FIG. 80A represents normal tissue from left to right as follows: salivary gland (1), bone marrow (2), tonsil (3), fetal liver (4), blood (5), bladder (6), thymus (7), spleen (8), adrenal gland (9), fetal brain (10), small intestine (11), testes (12), heart (13), colon (14), lung (15), prostate (16), brain cerebellum (17), skeletal muscle (18), kidney (19), pancreas (20), placenta (21), uterus (22) and mammary gland (23). The panel in FIG. 80B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 81A-81D show microarray data showing the expression of TAHO10 in normal samples and in diseased samples, such as significant expression in NHL samples and multiple myeloma samples. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 82A-82D show microarray data showing the expression of TAHO11 in normal samples and in diseased samples, such as significant expression in NHL samples, follicular lymphoma (FL), normal lymph node (NLN), normal b cells (NB), centroblasts and follicular mantle cells and normal spleen and normal tonsil. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 83A-83D show microarray data showing the expression of TAHO12 in normal samples and in diseased samples, such as significant expression in normal B cells, multiple myeloma and normal prostate. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth

muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 84A-84B show microarray data showing the expression of TAHO13 in normal samples and in diseased samples, such as significant expression in multiple myeloma and normal blood. FIGS. 84A-84B are shown as two panels. The panel in FIG. 84A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 84B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 85A-85D show microarray data showing the expression of TAHO15 in normal samples and in diseased samples, such as significant expression in NHL samples. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 86A-86D show microarray data showing the expression of TAHO17 in normal samples and in diseased samples, such as significant expression in normal B cells (NB) and memory B cells (mem B). Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 87A-87D show microarray data showing the expression of TAHO18 in normal samples and in diseased samples, such as significant expression in NHL samples. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 88A-88D show microarray data showing the expression of TAHO20 in normal samples and in diseased samples, such as significant expression in multiple myeloma (MM), normal B cells (NB) and normal colon, placenta, lung and spleen and bone marrow plasma cells (BM PC). Abbreviations used in the Figures are designated as follows: Non-

Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 89A-89D show microarray data showing the expression of TAHO21 in normal samples and in diseased samples, such as significant expression in NHL samples, centrocytes and memory B cell abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 90A-90D show microarray data showing the expression of TAHO25 in normal samples and in diseased samples, such as significant expression in NHL samples, normal lymph node, centroblasts, centrocytes and memory B cells and in normal tonsil and spleen. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 91A-91D show microarray data showing the expression of TAHO26 in normal samples and in diseased samples, such as significant expression in normal B cells. Abbreviations used in the Figures are designated as follows: Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), multiple myeloma cells (MM), small intestine (s. intestine), fetal liver (f. liver), smooth muscle (s. muscle), fetal brain (f. brain), natural killer cells (NK), neutrophils (N'phil), dendrocytes (DC), memory B cells (mem B), plasma cells (PC), bone marrow plasma cells (BM PC).

FIGS. 92A-92B show microarray data showing the expression of TAHO27 in normal samples and in diseased samples, such as significant expression in in multiple myeloma. FIGS. 92A-92D are shown as two panels. The panel in FIG. 92A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (1), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 92B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 93A-93B show microarray data showing the expression of TAHO28 in normal samples and in diseased samples,

such as significant expression in normal plasma cells and in multiple myeloma. FIGS. 93A-93B are shown as two panels. The panel in FIG. 93A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 93B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 94A-94B show microarray data showing the expression of TAHO29 in normal samples and in diseased samples, such as significant expression in in multiple myeloma, normal plasma cells and normal testes. FIGS. 94A-94B are shown as two panels. The panel in FIG. 94A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (1), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 94B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 95A-95B show microarray data showing the expression of TAHO30 in normal samples and in diseased samples, such as significant expression in in multiple myeloma and normal testes. FIGS. 95A-95B are shown as two panels. The panel in FIG. 95A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 95B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma

bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 96A-96B show microarray data showing the expression of TAHO31 in normal samples and in diseased samples, such as significant expression in in multiple myeloma, plasma cells and normal brain cerebellum. FIGS. 96A-96B are shown as two panels. The panel in FIG. 96A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 96B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 97A-97B show microarray data showing the expression of TAHO32 in normal samples and in diseased samples, such as significant expression in in multiple myeloma and normal prostate. FIGS. 97A-97B are shown as two panels. The panel in FIG. 97A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 97B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 98A-98B show microarray data showing the expression of TAHO33 in normal samples and in diseased samples, such as significant expression in in multiple myeloma. FIGS. 98A-98B are shown as two panels. The panel in FIG. 98A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 98B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39),

CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 99A-99B show microarray data showing the expression of TAHO34 in normal samples and in diseased samples, such as significant expression in in multiple myeloma, normal plasma cells and normal blood. FIGS. 98A-98B are shown as two panels. The panel in FIG. 94A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 94B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIGS. 100A-100B show microarray data showing the expression of TAHO35 in normal samples and in diseased samples, such as significant expression in in multiple myeloma. FIGS. 100A-100B are shown as two panels. The panel in FIG. 100A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 100B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

FIG. 101 show microarray data showing the expression of TAHO36 in normal samples and in diseased samples, such as significant expression in in multiple myeloma. FIGS. 101A-101B are shown as two panels. The panel in FIG. 101A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 101B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B

cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

I. Definitions

The terms "TAHO polypeptide" and "TAHO" as used herein and when immediately followed by a numerical designation, refer to various polypeptides, wherein the complete designation (i.e., TAHO/number) refers to specific polypeptide sequences as described herein. The terms "TAHO/number polypeptide" and "TAHO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides, polypeptide variants and fragments of native sequence polypeptides and polypeptide variants (which are further defined herein). The TAHO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods. The term "TAHO polypeptide" refers to each individual TAHO/number polypeptide disclosed herein. All disclosures in this specification which refer to the "TAHO polypeptide" refer to each of the polypeptides individually as well as jointly. For example, descriptions of the preparation of, purification of, derivation of, formation of antibodies to or against, formation of TAHO binding oligopeptides to or against, formation of TAHO binding organic molecules to or against, administration of, compositions containing, treatment of a disease with, etc., pertain to each polypeptide of the invention individually. The term "TAHO polypeptide" also includes variants of the TAHO/number polypeptides disclosed herein.

"TAHO1" is also herein referred to as "RP105", "CD180" or "LY64". "TAHO2" is also herein referred to as "CD20" or "MS4A1". "TAHO3" is also herein referred to as "FcRH2" or "SPAP1". "TAHO4" is also herein referred to as "CD79A". "TAHO5" is also herein referred to as "CD79B". "TAHO6" is also herein referred to as "CR2" or "CD21". "TAHO7" is also herein referred to as "CCR6". "TAHO8" is also herein referred to as "CD72". "TAHO9" is also herein referred to as "P2RX5" or "UNQ2170". "TAHO10" is also herein referred to as "HLA-DOB". "TAHO11" is also herein referred to as "CXCR5" or "BLR1". "TAHO12" is also herein referred to as "FCER2" or "CD23". "TAHO13" is also herein referred to as "GPR2" or "UNQ12100". "TAHO14" is also herein referred to as "BTig". "TAHO15" is also herein referred to as "NAG14" or "LRR4". "TAHO16" is also herein referred to as "SLGC16270". "TAHO17" is also herein referred to as "FcRH1" or "IRTA5". "TAHO18" is also herein referred to as "IRTA2" or "FcRH5". "TAHO19" is also herein referred to as "ATWD578". "TAHO20" is also herein referred to as "FcRH3" or "IRTA3". "TAHO21" is also herein referred to as "IRTA1" or "FcRH4". "TAHO22" is also herein referred to as "FcRH6" or "FAIL". "TAHO23" is also herein referred to as "BCMA". "TAHO24" is also herein referred to as "239287 at". "TAHO25" is also herein referred to as "CD19". "TAHO26" is also herein referred to as "CD22". "TAHO27" is also herein referred to as "CXCR3" or "UNQ8371". "TAHO28" is also herein referred to as "SILV" or

"UNQ1747". "TAHO29" is also herein referred to as "KCNK4" or "UNQ11492". "TAHO30" is also herein referred to as "CXorf1" or "UNQ9197". "TAHO31" is also herein referred to as "LRRN5" or "UNQ256". "TAHO32" is also herein referred to as "UNQ9308". "TAHO33" is also herein referred to as "IGSF4B" or "UNQ225". "TAHO34" is also herein referred to as "BC021178" or "UNQ13267". "TAHO35" is also herein referred to as "FLJ12681" or "UNQ6034". "TAHO36" is also herein referred to as "I_928646" or "UNQ12376".

A "native sequence TAHO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding TAHO polypeptide derived from nature. Such native sequence TAHO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence TAHO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific TAHO polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In certain embodiments of the invention, the native sequence TAHO polypeptides disclosed herein are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons (if indicated) are shown in bold font and underlined in the figures. Nucleic acid residues indicated as "N" in the accompanying figures are any nucleic acid residue. However, while the TAHO polypeptides disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the amino acid position 1 in the figures may be employed as the starting amino acid residue for the TAHO polypeptides.

The TAHO polypeptide "extracellular domain" or "ECD" refers to a form of the TAHO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a TAHO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the TAHO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a TAHO polypeptide may contain from about 5 or fewer amino acids on either side of the transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

The approximate location of the "signal peptides" of the various TAHO polypeptides disclosed herein may be shown in the present specification and/or the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (e.g., Nielsen et al., *Prot. Eng.* 10:1-6 (1997) and von Heinje et al., *Nucl. Acids. Res.* 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a

secreted polypeptide is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present invention.

“TAHO polypeptide variant” means a TAHO polypeptide, preferably an active TAHO polypeptide, as defined herein having at least about 80% amino acid sequence identity with a full-length native sequence TAHO polypeptide sequence as disclosed herein, a TAHO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a TAHO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length TAHO polypeptide sequence as disclosed herein (such as those encoded by a nucleic acid that represents only a portion of the complete coding sequence for a full-length TAHO polypeptide). Such TAHO polypeptide variants include, for instance, TAHO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a TAHO polypeptide variant will have at least about 80% amino acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% amino acid sequence identity, to a full-length native sequence TAHO polypeptide sequence as disclosed herein, a TAHO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a TAHO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length TAHO polypeptide sequence as disclosed herein. Ordinarily, TAHO variant polypeptides are at least about 10 amino acids in length, alternatively at least about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600 amino acids in length, or more. Optionally, TAHO variant polypeptides will have no more than one conservative amino acid substitution as compared to the native TAHO polypeptide sequence, alternatively no more than 2, 3, 4, 5, 6, 7, 8, 9, or 10 conservative amino acid substitution as compared to the native TAHO polypeptide sequence.

“Percent (% amino acid sequence identity)” with respect to the TAHO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific TAHO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the

U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, Calif. or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } \frac{X}{Y}$$

where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this method, Tables 2 and 3 demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated “Comparison Protein” to the amino acid sequence designated “TAHO”, wherein “TAHO” represents the amino acid sequence of a hypothetical TAHO polypeptide of interest, “Comparison Protein” represents the amino acid sequence of a polypeptide against which the “TAHO” polypeptide of interest is being compared, and “X,” “Y” and “Z” each represent different hypothetical amino acid residues. Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

“TAHO variant polynucleotide” or “TAHO variant nucleic acid sequence” means a nucleic acid molecule which encodes a TAHO polypeptide, preferably an active TAHO polypeptide, as defined herein and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence TAHO polypeptide sequence as disclosed herein, a full-length native sequence TAHO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a TAHO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length TAHO polypeptide sequence as disclosed herein (such as those encoded by a nucleic acid that represents only a portion of the complete coding sequence for a full-length TAHO polypeptide). Ordinarily, a TAHO variant polynucleotide will have at least about 80% nucleic acid sequence identity, alternatively at least about 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% nucleic acid sequence identity with a nucleic acid sequence encoding a full-length native sequence TAHO polypeptide sequence as disclosed herein, a full-length native sequence TAHO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a TAHO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length TAHO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

Ordinarily, TAHO variant polynucleotides are at least about 5 nucleotides in length, alternatively at least about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 15, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 610, 620, 630, 640, 650, 660, 670, 680, 690, 700, 710, 720, 730, 740, 750, 760, 770, 780, 790, 800, 810, 820, 830, 840, 850, 860, 870, 880, 890, 900, 910, 920, 930, 940, 950, 960, 970, 980, 990, or 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length.

"Percent (%) nucleic acid sequence identity" with respect to TAHO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the TAHO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, Calif. or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "TAHO-DNA", wherein "TAHO-DNA" represents a hypothetical TAHO-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which

the "TAHO-DNA" nucleic acid molecule of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides. Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

In other embodiments, TAHO variant polynucleotides are nucleic acid molecules that encode a TAHO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length TAHO polypeptide as disclosed herein. TAHO variant polypeptides may be those that are encoded by a TAHO variant polynucleotide.

The term "full-length coding region" when used in reference to a nucleic acid encoding a TAHO polypeptide refers to the sequence of nucleotides which encode the full-length TAHO polypeptide of the invention (which is often shown between start and stop codons, inclusive thereof, in the accompanying figures). The term "full-length coding region" when used in reference to an ATCC deposited nucleic acid refers to the TAHO polypeptide-encoding portion of the cDNA that is inserted into the vector deposited with the ATCC (which is often shown between start and stop codons, inclusive thereof, in the accompanying figures (start and stop codons are bolded and underlined in the figures)).

"Isolated," when used to describe the various TAHO polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide in situ within recombinant cells, since at least one component of the TAHO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated" TAHO polypeptide-encoding nucleic acid or other polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the polypeptide-encoding nucleic acid. An isolated polypeptide-encoding nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated polypeptide-encoding nucleic acid molecules therefore are distinguished from the specific polypeptide-encoding nucleic acid molecule as it exists in natural cells. However, an isolated polypeptide-encoding nucleic acid molecule includes polypeptide-encoding nucleic acid molecules contained in cells that ordinarily express the polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence.

For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., *Current Protocols in Molecular Biology*, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50° C.; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42° C.; or (3) overnight hybridization in a solution that employs 50% formamide, 5×SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5×Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42° C., with a 10 minute wash at 42° C. in 0.2×SSC (sodium chloride/sodium citrate) followed by a 10 minute high-stringency wash consisting of 0.1×SSC containing EDTA at 55° C.

"Moderately stringent conditions" may be identified as described by Sambrook et al., *Molecular Cloning: A Laboratory Manual*, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and % SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37° C. in a solution comprising: 20% formamide, 5×SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5×Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1×SSC at about 37-50° C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a TAHO polypeptide or anti-TAHO antibody fused to a "tag polypeptide". The tag

polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

"Active" or "activity" for the purposes herein refers to form(s) of a TAHO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring TAHO, wherein "biological" activity refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring TAHO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring TAHO and an "immunological" activity refers to the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring TAHO.

The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native TAHO polypeptide disclosed herein. In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics a biological activity of a native TAHO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native TAHO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for identifying agonists or antagonists of a TAHO polypeptide may comprise contacting a TAHO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the TAHO polypeptide.

"Treating" or "treatment" or "alleviation" refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented. A subject or mammal is successfully "treated" for a TAHO polypeptide-expressing cancer if, after receiving a therapeutic amount of an anti-TAHO antibody, TAHO binding oligopeptide or TAHO binding organic molecule according to the methods of the present invention, the patient shows observable and/or measurable reduction in or absence of one or more of the following: reduction in the number of cancer cells or absence of the cancer cells; reduction in the tumor size; inhibition (i.e., slow to some extent and preferably stop) of cancer cell infiltration into peripheral organs including the spread of cancer into soft tissue and bone; inhibition (i.e., slow to some extent and preferably stop) of tumor metastasis; inhibition, to some extent, of tumor growth; and/or relief to some extent, one or more of the symptoms associated with the specific cancer; reduced morbidity and mortality, and improvement in quality of life issues. To the extent the anti-TAHO antibody or TAHO binding oligopeptide may prevent growth and/or kill existing cancer cells, it may be cytostatic and/or cytotoxic. Reduction of these signs or symptoms may also be felt by the patient.

The above parameters for assessing successful treatment and improvement in the disease are readily measurable by routine procedures familiar to a physician. For cancer therapy, efficacy can be measured, for example, by assessing the time to disease progression (TTP) and/or determining the

response rate (RR). Metastasis can be determined by staging tests and by bone scan and tests for calcium level and other enzymes to determine spread to the bone. CT scans can also be done to look for spread to the pelvis and lymph nodes in the area. Chest X-rays and measurement of liver enzyme levels by known methods are used to look for metastasis to the lungs and liver, respectively. Other routine methods for monitoring the disease include transrectal ultrasonography (TRUS) and transrectal needle biopsy (TRNB).

For bladder cancer, which is a more localized cancer, methods to determine progress of disease include urinary cytologic evaluation by cystoscopy, monitoring for presence of blood in the urine, visualization of the urothelial tract by sonography or an intravenous pyelogram, computed tomography (CT) and magnetic resonance imaging (MRI). The presence of distant metastases can be assessed by CT of the abdomen, chest x-rays, or radionuclide imaging of the skeleton.

“Chronic” administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. “Intermittent” administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

“Mammal” for purposes of the treatment of, alleviating the symptoms of a cancer refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

Administration “in combination with” one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

“Carriers” as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN®, polyethylene glycol (PEG), and PLURONICS®.

By “solid phase” or “solid support” is meant a non-aqueous matrix to which an antibody, TAHO binding oligopeptide or TAHO binding organic molecule of the present invention can adhere or attach. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Pat. No. 4,275,149.

A “liposome” is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a TAHO polypeptide, an antibody thereto or a TAHO binding oligopeptide) to a mammal. The

components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

A “small” molecule or “small” organic molecule is defined herein to have a molecular weight below about 500 Daltons.

An “effective amount” of a polypeptide, antibody, TAHO binding oligopeptide, TAHO binding organic molecule or an agonist or antagonist thereof as disclosed herein is an amount sufficient to carry out a specifically stated purpose. An “effective amount” may be determined empirically and in a routine manner, in relation to the stated purpose.

The term “therapeutically effective amount” refers to an amount of an antibody, polypeptide, TAHO binding oligopeptide, TAHO binding organic molecule or other drug effective to “treat” a disease or disorder in a subject or mammal. In the case of cancer, the therapeutically effective amount of the drug may reduce the number of cancer cells; reduce the tumor size; inhibit (i.e., slow to some extent and preferably stop) cancer cell infiltration into peripheral organs; inhibit (i.e., slow to some extent and preferably stop) tumor metastasis; inhibit, to some extent, tumor growth; and/or relieve to some extent one or more of the symptoms associated with the cancer. See the definition herein of “treating”. To the extent the drug may prevent growth and/or kill existing cancer cells, it may be cytostatic and/or cytotoxic.

A “growth inhibitory amount” of an anti-TAHO antibody, TAHO polypeptide, TAHO binding oligopeptide or TAHO binding organic molecule is an amount capable of inhibiting the growth of a cell, especially tumor, e.g., cancer cell, either in vitro or in vivo. A “growth inhibitory amount” of an anti-TAHO antibody, TAHO polypeptide, TAHO binding oligopeptide or TAHO binding organic molecule for purposes of inhibiting neoplastic cell growth may be determined empirically and in a routine manner.

A “cytotoxic amount” of an anti-TAHO antibody, TAHO polypeptide, TAHO binding oligopeptide or TAHO binding organic molecule is an amount capable of causing the destruction of a cell, especially tumor, e.g., cancer cell, either in vitro or in vivo. A “cytotoxic amount” of an anti-TAHO antibody, TAHO polypeptide, TAHO binding oligopeptide or TAHO binding organic molecule for purposes of inhibiting neoplastic cell growth may be determined empirically and in a routine manner.

The term “antibody” is used in the broadest sense and specifically covers, for example, single anti-TAHO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-TAHO antibody compositions with polypepitopic specificity, polyclonal antibodies, single chain anti-TAHO antibodies, and fragments of anti-TAHO antibodies (see below) as long as they exhibit the desired biological or immunological activity. The term “immunoglobulin” (Ig) is used interchangeable with antibody herein.

An “isolated antibody” is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at

least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

The basic 4-chain antibody unit is a heterotetrameric glycoprotein composed of two identical light (L) chains and two identical heavy (H) chains (an IgM antibody consists of 5 of the basic heterotetramer unit along with an additional polypeptide called J chain, and therefore contain 10 antigen binding sites, while secreted IgA antibodies can polymerize to form polyvalent assemblies comprising 2-5 of the basic 4-chain units along with J chain). In the case of IgGs, the 4-chain unit is generally about 150,000 daltons. Each L chain is linked to a H chain by one covalent disulfide bond, while the two H chains are linked to each other by one or more disulfide bonds depending on the H chain isotype. Each H and L chain also has regularly spaced intrachain disulfide bridges. Each H chain has at the N-terminus, a variable domain (V_H) followed by three constant domains (C_H) for each of the α and γ chains and four C_H domains for μ and ϵ isotypes. Each L chain has at the N-terminus, a variable domain (V_L) followed by a constant domain (C_L) at its other end. The V_L is aligned with the V_H and the C_L is aligned with the first constant domain of the heavy chain (C_H1). Particular amino acid residues are believed to form an interface between the light chain and heavy chain variable domains. The pairing of a V_H and V_L together forms a single antigen-binding site. For the structure and properties of the different classes of antibodies, see, e.g., *Basic and Clinical Immunology*, 8th edition, Daniel P. Stites, Abba I. Terr and Tristram G. Parslow (eds.), Appleton & Lange, Norwalk, Conn., 1994, page 71 and Chapter 6.

The L chain from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains. Depending on the amino acid sequence of the constant domain of their heavy chains (C_H), immunoglobulins can be assigned to different classes or isotypes. There are five classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, having heavy chains designated α , δ , ϵ , γ , and μ , respectively. The γ and α classes are further divided into subclasses on the basis of relatively minor differences in C_H sequence and function, e.g., humans express the following subclasses: IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

The term "variable" refers to the fact that certain segments of the variable domains differ extensively in sequence among antibodies. The V domain mediates antigen binding and define specificity of a particular antibody for its particular antigen. However, the variability is not evenly distributed across the 110-amino acid span of the variable domains. Instead, the V regions consist of relatively invariant stretches called framework regions (FRs) of 15-30 amino acids separated by shorter regions of extreme variability called "hypervariable regions" that are each 9-12 amino acids long. The variable domains of native heavy and light chains each comprise four FRs, largely adopting a β -sheet configuration, connected by three hypervariable regions, which form loops connecting, and in some cases forming part of, the β -sheet structure. The hypervariable regions in each chain are held together in close proximity by the FRs and, with the hypervariable regions from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody dependent cellular cytotoxicity (ADCC).

The term "hypervariable region" when used herein refers to the amino acid residues of an antibody which are responsible for antigen-binding. The hypervariable region generally comprises amino acid residues from a "complementarity determining region" or "CDR" (e.g. around about residues 24-34 (L1), 50-56 (L2) and 89-97 (L3) in the V_L , and around about 1-35 (H1), 50-65 (H2) and 95-102 (H3) in the V_H ; Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)) and/or those residues from a "hypervariable loop" (e.g. residues 26-32 (L1), 50-52 (L2) and 91-96 (L3) in the V_L , and 26-32 (H1), 53-55 (H2) and 96-101 (H3) in the V_H ; Chothia and Lesk *J. Mol. Biol.* 196:901-917 (1987)).

The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to polyclonal antibody preparations which include different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they may be synthesized uncontaminated by other antibodies. The modifier "monoclonal" is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies useful in the present invention may be prepared by the hybridoma methodology first described by Kohler et al., *Nature*, 256:495 (1975), or may be made using recombinant DNA methods in bacterial, eukaryotic animal or plant cells (see, e.g., U.S. Pat. No. 4,816,567). The "monoclonal antibodies" may also be isolated from phage antibody libraries using the techniques described in Clackson et al., *Nature*, 352:624-628 (1991) and Marks et al., *J. Mol. Biol.*, 222:581-597 (1991), for example.

The monoclonal antibodies herein include "chimeric" antibodies in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (see U.S. Pat. No. 4,816,567; and Morrison et al., *Proc. Natl. Acad. Sci. USA*, 81:6851-6855 (1984)). Chimeric antibodies of interest herein include "primatized" antibodies comprising variable domain antigen-binding sequences derived from a non-human primate (e.g. Old World Monkey, Ape etc), and human constant region sequences.

An "intact" antibody is one which comprises an antigen-binding site as well as a C_L and at least heavy chain constant domains, C_H1 , C_H2 and C_H3 . The constant domains may be native sequence constant domains (e.g. human native sequence constant domains) or amino acid sequence variant thereof. Preferably, the intact antibody has one or more effector functions.

"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv fragments; diabodies; linear antibodies (see U.S. Pat. No. 5,641,870, Example 2; Zapata et al., *Pro-*

tein Eng. 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. The Fab fragment consists of an entire L chain along with the variable region domain of the H chain (V_H), and the first constant domain of one heavy chain (C_{H1}). Each Fab fragment is monovalent with respect to antigen binding, i.e., it has a single antigen-binding site. Pepsin treatment of an antibody yields a single large $F(ab')_2$ fragment which roughly corresponds to two disulfide linked Fab fragments having divalent antigen-binding activity and is still capable of cross-linking antigen. Fab' fragments differ from Fab fragments by having additional few residues at the carboxy terminus of the C_{H1} domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The Fc fragment comprises the carboxy-terminal portions of both H chains held together by disulfides. The effector functions of antibodies are determined by sequences in the Fc region, which region is also the part recognized by Fc receptors (FcR) found on certain types of cells.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and binding site. This fragment consists of a dimer of one heavy- and one light-chain variable region domain in tight, non-covalent association. From the folding of these two domains emanate six hypervariable loops (3 loops each from the H and L chain) that contribute the amino acid residues for antigen binding and confer antigen binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

"Single-chain Fv" also abbreviated as "sFv" or "scFv" are antibody fragments that comprise the V_H and V_L antibody domains connected into a single polypeptide chain. Preferably, the sFv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994); Borrebaeck 1995, infra.

The term "diabodies" refers to small antibody fragments prepared by constructing sFv fragments (see preceding paragraph) with short linkers (about 5-10 residues) between the V_H and V_L domains such that inter-chain but not intra-chain pairing of the V domains is achieved, resulting in a bivalent fragment, i.e., fragment having two antigen-binding sites. Bispecific diabodies are heterodimers of two "crossover" sFv fragments in which the V_H and V_L domains of the two antibodies are present on different polypeptide chains. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

"Humanized" forms of non-human (e.g., rodent) antibodies are chimeric antibodies that contain minimal sequence derived from the non-human antibody. For the most part, humanized antibodies are human immunoglobulins (recipient antibody) in which residues from a hypervariable region

of the recipient are replaced by residues from a hypervariable region of a non-human species (donor antibody) such as mouse, rat, rabbit or non-human primate having the desired antibody specificity, affinity, and capability. In some instances, framework region (FR) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, humanized antibodies may comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications are made to further refine antibody performance. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the hypervariable loops correspond to those of a non-human immunoglobulin and all or substantially all of the FRs are those of a human immunoglobulin sequence. The humanized antibody optionally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332: 323-329 (1988); and Presta, *Curr. Op. Struct. Biol.* 2:593-596 (1992).

A "species-dependent antibody," e.g., a mammalian anti-human IgE antibody, is an antibody which has a stronger binding affinity for an antigen from a first mammalian species than it has for a homologue of that antigen from a second mammalian species. Normally, the species-dependent antibody "bind specifically" to a human antigen (i.e., has a binding affinity (Kd) value of no more than about 1×10^{-7} M, preferably no more than about 1×10^{-8} and most preferably no more than about 1×10^{-9} M) but has a binding affinity for a homologue of the antigen from a second non-human mammalian species which is at least about 50 fold, or at least about 500 fold, or at least about 1000 fold, weaker than its binding affinity for the human antigen. The species-dependent antibody can be of any of the various types of antibodies as defined above, but preferably is a humanized or human antibody.

A "TAHO binding oligopeptide" is an oligopeptide that binds, preferably specifically, to a TAHO polypeptide as described herein. TAHO binding oligopeptides may be chemically synthesized using known oligopeptide synthesis methodology or may be prepared and purified using recombinant technology. TAHO binding oligopeptides are usually at least about 5 amino acids in length, alternatively at least about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 amino acids in length or more, wherein such oligopeptides that are capable of binding, preferably specifically, to a TAHO polypeptide as described herein. TAHO binding oligopeptides may be identified without undue experimentation using well known techniques. In this regard, it is noted that techniques for screening oligopeptide libraries for oligopeptides that are capable of specifically binding to a polypeptide target are well known in the art (see, e.g., U.S. Pat. Nos. 5,556,762, 5,750,373, 4,708, 871, 4,833,092, 5,223,409, 5,403,484, 5,571,689, 5,663,143; PCT Publication Nos. WO 84/03506 and WO84/03564; Geysen et al., Proc. Natl. Acad. Sci. U.S.A., 81:3998-4002 (1984); Geysen et al., Proc. Natl. Acad. Sci. U.S.A., 82:178-182 (1985); Geysen et al., in *Synthetic Peptides as Antigens*, 130-149 (1986); Geysen et al., *J. Immunol. Meth.*, 102:259-274 (1987); Schoofs et al., *J. Immunol.* 140:611-616 (1988), Cwirla, S. E. et al. (1990) Proc. Natl. Acad. Sci. USA, 87:6378; Lowman, H. B. et al. (1991) *Biochemistry*,

30:10832; Clackson, T. et al. (1991) *Nature*, 352: 624; Marks, J. D. et al. (1991), *J. Mol. Biol.*, 222:581; Kang, A. S. et al. (1991) *Proc. Natl. Acad. Sci. USA*, 88:8363, and Smith, G. P. (1991) *Current Opin. Biotechnol.*, 2:668).

A "TAHO binding organic molecule" is an organic molecule other than an oligopeptide or antibody as defined herein that binds, preferably specifically, to a TAHO polypeptide as described herein. TAHO binding organic molecules may be identified and chemically synthesized using known methodology (see, e.g., PCT Publication Nos. WO00/00823 and WO00/39585). TAHO binding organic molecules are usually less than about 2000 daltons in size, alternatively less than about 1500, 750, 500, 250 or 200 daltons in size, wherein such organic molecules that are capable of binding, preferably specifically, to a TAHO polypeptide as described herein may be identified without undue experimentation using well known techniques. In this regard, it is noted that techniques for screening organic molecule libraries for molecules that are capable of binding to a polypeptide target are well known in the art (see, e.g., PCT Publication Nos. WO00/00823 and WO00/39585).

An antibody, oligopeptide or other organic molecule "which binds" an antigen of interest, e.g. a tumor-associated polypeptide antigen target, is one that binds the antigen with sufficient affinity such that the antibody, oligopeptide or other organic molecule is useful as a therapeutic agent in targeting a cell or tissue expressing the antigen, and does not significantly cross-react with other proteins. In such embodiments, the extent of binding of the antibody, oligopeptide or other organic molecule to a "non-target" protein will be less than about 10% of the binding of the antibody, oligopeptide or other organic molecule to its particular target protein as determined by fluorescence activated cell sorting (FACS) analysis or radioimmunoprecipitation (RIA). With regard to the binding of an antibody, oligopeptide or other organic molecule to a target molecule, the term "specific binding" or "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide target means binding that is measurably different from a non-specific interaction. Specific binding can be measured, for example, by determining binding of a molecule compared to binding of a control molecule, which generally is a molecule of similar structure that does not have binding activity. For example, specific binding can be determined by competition with a control molecule that is similar to the target, for example, an excess of non-labeled target. In this case, specific binding is indicated if the binding of the labeled target to a probe is competitively inhibited by excess unlabeled target. The term "specific binding" or "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a particular polypeptide target as used herein can be exhibited, for example, by a molecule having a Kd for the target of at least about 10^{-4} M, alternatively at least about 10^{-5} M, alternatively at least about 10^{-6} M, alternatively at least about 10^{-7} M, alternatively at least about 10^{-8} M, alternatively at least about 10^{-9} M, alternatively at least about 10^{-10} M, alternatively at least about 10^{-11} M, alternatively at least about 10^{-12} M, or greater. In one embodiment, the term "specific binding" refers to binding where a molecule binds to a particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope.

An antibody, oligopeptide or other organic molecule that "inhibits the growth of tumor cells expressing a TAHO polypeptide" or a "growth inhibitory" antibody, oligopeptide or other organic molecule is one which results in measurable growth inhibition of cancer cells expressing or overexpressing the appropriate TAHO polypeptide. The TAHO polypep-

5 tide may be a transmembrane polypeptide expressed on the surface of a cancer cell or may be a polypeptide that is produced and secreted by a cancer cell. Preferred growth inhibitory anti-TAHO antibodies, oligopeptides or organic molecules inhibit growth of TAHO-expressing tumor cells by greater than 20%, preferably from about 20% to about 50%, and even more preferably, by greater than 50% (e.g., from about 50% to about 100%) as compared to the appropriate control, the control typically being tumor cells not treated with the antibody, oligopeptide or other organic molecule being tested. In one embodiment, growth inhibition can be measured at an antibody concentration of about 0.1 to 30 $\mu\text{g/ml}$ or about 0.5 nM to 200 nM in cell culture, where the growth inhibition is determined 1-10 days after exposure of the tumor cells to the antibody. Growth inhibition of tumor cells in vivo can be determined in various ways such as is described in the Experimental Examples section below. The antibody is growth inhibitory in vivo if administration of the anti-TAHO antibody at about 1 $\mu\text{g/kg}$ to about 100 mg/kg body weight results in reduction in tumor size or tumor cell proliferation within about 5 days to 3 months from the first administration of the antibody, preferably within about 5 to 30 days.

An antibody, oligopeptide or other organic molecule which "induces apoptosis" is one which induces programmed cell death as determined by binding of annexin V, fragmentation of DNA, cell shrinkage, dilation of endoplasmic reticulum, cell fragmentation, and/or formation of membrane vesicles (called apoptotic bodies). The cell is usually one which over-expresses a TAHO polypeptide. Preferably the cell is a tumor cell, e.g., a hematopoietic cell, such as a B cell, T cell, basophil, eosinophil, neutrophil, monocyte, platelet or erythrocyte. Various methods are available for evaluating the cellular events associated with apoptosis. For example, phosphatidyl serine (PS) translocation can be measured by annexin binding; DNA fragmentation can be evaluated through DNA laddering; and nuclear/chromatin condensation along with DNA fragmentation can be evaluated by any increase in hypodiploid cells. Preferably, the antibody, oligopeptide or other organic molecule which induces apoptosis is one which results in about 2 to 50 fold, preferably about 5 to 50 fold, and most preferably about 10 to 50 fold, induction of annexin binding relative to untreated cell in an annexin binding assay.

Antibody "effector functions" refer to those biological activities attributable to the Fc region (a native sequence Fc region or amino acid sequence variant Fc region) of an antibody, and vary with the antibody isotype. Examples of antibody effector functions include: C1q binding and complement dependent cytotoxicity; Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (e.g., B cell receptor); and B cell activation.

"Antibody-dependent cell-mediated cytotoxicity" or "ADCC" refers to a form of cytotoxicity in which secreted Ig bound onto Fc receptors (FcRs) present on certain cytotoxic cells (e.g., Natural Killer (NK) cells, neutrophils, and macrophages) enable these cytotoxic effector cells to bind specifically to an antigen-bearing target cell and subsequently kill the target cell with cytotoxins. The antibodies "arm" the cytotoxic cells and are absolutely required for such killing. The primary cells for mediating ADCC, NK cells, express Fc γ RIII only, whereas monocytes express Fc γ RI, Fc γ RII and Fc γ RIII. FcR expression on hematopoietic cells is summarized in Table 3 on page 464 of Ravetch and Kinet, *Annu. Rev. Immunol.* 9:457-92 (1991). To assess ADCC activity of a molecule of interest, an in vitro ADCC assay, such as that described in U.S. Pat. No. 5,500,362 or 5,821,337 may be

performed. Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest may be assessed in vivo, e.g., in an animal model such as that disclosed in Clynes et al. (USA) 95:652-656 (1998).

“Fc receptor” or “FcR” describes a receptor that binds to the Fc region of an antibody. The preferred FcR is a native sequence human FcR. Moreover, a preferred FcR is one which binds an IgG antibody (a gamma receptor) and includes receptors of the FcγRI, FcγRII and FcγRIII subclasses, including allelic variants and alternatively spliced forms of these receptors. FcγRII receptors include FcγRIIA (an “activating receptor”) and FcγRIIB (an “inhibiting receptor”), which have similar amino acid sequences that differ primarily in the cytoplasmic domains thereof. Activating receptor FcγRIIA contains an immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic domain. Inhibiting receptor FcγRIIB contains an immunoreceptor tyrosine-based inhibition motif (ITIM) in its cytoplasmic domain. (see review M. in Daëron, *Annu. Rev. Immunol.* 15:203-234 (1997)). FcRs are reviewed in Ravetch and Kinetic, *Annu. Rev. Immunol.* 9:457-492 (1991); Capel et al., *Immunomethods* 4:25-34 (1994); and de Haas et al., *J. Lab. Clin. Med.* 126:330-41 (1995). Other FcRs, including those to be identified in the future, are encompassed by the term “FcR” herein. The term also includes the neonatal receptor, FcRn, which is responsible for the transfer of maternal IgGs to the fetus (Guyer et al., *J. Immunol.* 117:587 (1976) and Kim et al., *J. Immunol.* 24:249 (1994)).

“Human effector cells” are leukocytes which express one or more FcRs and perform effector functions. Preferably, the cells express at least FcγRIII and perform ADCC effector function. Examples of human leukocytes which mediate ADCC include peripheral blood mononuclear cells (PBMC), natural killer (NK) cells, monocytes, cytotoxic T cells and neutrophils; with PBMCs and NK cells being preferred. The effector cells may be isolated from a native source, e.g., from blood.

“Complement dependent cytotoxicity” or “CDC” refers to the lysis of a target cell in the presence of complement. Activation of the classical complement pathway is initiated by the binding of the first component of the complement system (C1q) to antibodies (of the appropriate subclass) which are bound to their cognate antigen. To assess complement activation, a CDC assay, e.g., as described in Gazzano-Santoro et al., *Immunol. Methods* 202:163 (1996), may be performed.

The terms “cancer” and “cancerous” refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth. Examples of cancer include, but are not limited to, hematopoietic cancers or blood-related cancers, such as lymphoma, leukemia, myeloma or lymphoid malignancies, but also cancers of the spleen and cancers of the lymph nodes. More particular examples of such B-cell associated cancers, including for example, high, intermediate and low grade lymphomas (including B cell lymphomas such as, for example, mucosa-associated-lymphoid tissue B cell lymphoma and non-Hodgkin’s lymphoma, mantle cell lymphoma, Burkitt’s lymphoma, small lymphocytic lymphoma, marginal zone lymphoma, diffuse large cell lymphoma, follicular lymphoma, and Hodgkin’s lymphoma and T cell lymphomas) and leukemias (including secondary leukemia, chronic lymphocytic leukemia, such as B cell leukemia (CD5+ B lymphocytes), myeloid leukemia, such as acute myeloid leukemia, chronic myeloid leukemia, lymphoid leukemia, such as

acute lymphoblastic leukemia and myelodysplasia), multiple myeloma, such as plasma cell malignancy, and other hematological and/or B cell- or T-cell-associated cancers. Also included are cancers of additional hematopoietic cells, including polymorphonuclear leukocytes, such as basophils, eosinophils, neutrophils and monocytes, dendritic cells, platelets, erythrocytes and natural killer cells. The origins of B-cell cancers are as follows: marginal zone B-cell lymphoma originates in memory B-cells in marginal zone, follicular lymphoma and diffuse large B-cell lymphoma originates in centrocytes in the light zone of germinal centers, multiple myeloma originates in plasma cells, chronic lymphocytic leukemia and small lymphocytic leukemia originates in B1 cells (CD5+), mantle cell lymphoma originates in naive B-cells in the mantle zone and Burkitt’s lymphoma originates in centroblasts in the dark zone of germinal centers. Tissues which include hematopoietic cells referred herein to as “hematopoietic cell tissues” include thymus and bone marrow and peripheral lymphoid tissues, such as spleen, lymph nodes, lymphoid tissues associated with mucosa, such as the gut-associated lymphoid tissues, tonsils, Peyer’s patches and appendix and lymphoid tissues associated with other mucosa, for example, the bronchial linings.

The terms “cell proliferative disorder” and “proliferative disorder” refer to disorders that are associated with some degree of abnormal cell proliferation. In one embodiment, the cell proliferative disorder is cancer.

“Tumor”, as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues.

An antibody, oligopeptide or other organic molecule which “induces cell death” is one which causes a viable cell to become nonviable. The cell is one which expresses a TAHO polypeptide and is of a cell type which specifically expresses or overexpresses a TAHO polypeptide. The cell may be cancerous or normal cells of the particular cell type. The TAHO polypeptide may be a transmembrane polypeptide expressed on the surface of a cancer cell or may be a polypeptide that is produced and secreted by a cancer cell. The cell may be a cancer cell, e.g., a B cell or T cell. Cell death in vitro may be determined in the absence of complement and immune effector cells to distinguish cell death induced by antibody-dependent cell-mediated cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC). Thus, the assay for cell death may be performed using heat inactivated serum (i.e., in the absence of complement) and in the absence of immune effector cells. To determine whether the antibody, oligopeptide or other organic molecule is able to induce cell death, loss of membrane integrity as evaluated by uptake of propidium iodide (PI), trypan blue (see Moore et al. *Cytotechnology* 17:1-11 (1995)) or 7AAD can be assessed relative to untreated cells. Preferred cell death-inducing antibodies, oligopeptides or other organic molecules are those which induce PI uptake in the PI uptake assay in BT474 cells.

A “TAHO-expressing cell” is a cell which expresses an endogenous or transfected TAHO polypeptide either on the cell surface or in a secreted form. A “TAHO-expressing cancer” is a cancer comprising cells that have a TAHO polypeptide present on the cell surface or that produce and secrete a TAHO polypeptide. A “TAHO-expressing cancer” optionally produces sufficient levels of TAHO polypeptide on the surface of cells thereof, such that an anti-TAHO antibody, oligopeptide to other organic molecule can bind thereto and have a therapeutic effect with respect to the cancer. In another embodiment, a “TAHO-expressing cancer” optionally produces and secretes sufficient levels of TAHO polypeptide, such that an anti-TAHO antibody, oligopeptide to other

organic molecule antagonist can bind thereto and have a therapeutic effect with respect to the cancer. With regard to the latter, the antagonist may be an antisense oligonucleotide which reduces, inhibits or prevents production and secretion of the secreted TAHO polypeptide by tumor cells. A cancer which "overexpresses" a TAHO polypeptide is one which has significantly higher levels of TAHO polypeptide at the cell surface thereof, or produces and secretes, compared to a noncancerous cell of the same tissue type. Such overexpression may be caused by gene amplification or by increased transcription or translation. TAHO polypeptide overexpression may be determined in a detection or prognostic assay by evaluating increased levels of the TAHO protein present on the surface of a cell, or secreted by the cell (e.g., via an immunohistochemistry assay using anti-TAHO antibodies prepared against an isolated TAHO polypeptide which may be prepared using recombinant DNA technology from an isolated nucleic acid encoding the TAHO polypeptide; FACS analysis, etc.). Alternatively, or additionally, one may measure levels of TAHO polypeptide-encoding nucleic acid or mRNA in the cell, e.g., via fluorescent in situ hybridization using a nucleic acid based probe corresponding to a TAHO-encoding nucleic acid or the complement thereof; (FISH; see WO98/45479 published October, 1998), Southern blotting, Northern blotting, or polymerase chain reaction (PCR) techniques; such as real time quantitative PCR (RT-PCR). One may also study TAHO polypeptide overexpression by measuring shed antigen in a biological fluid such as serum, e.g., using antibody-based assays (see also, e.g., U.S. Pat. No. 4,933,294 issued Jun. 12, 1990; WO91/05264 published Apr. 18, 1991; U.S. Pat. No. 5,401,638 issued Mar. 28, 1995; and Sias et al., *J. Immunol. Methods* 132:73-80 (1990)). Aside from the above assays, various in vivo assays are available to the skilled practitioner. For example, one may expose cells within the body of the patient to an antibody which is optionally labeled with a detectable label, e.g., a radioactive isotope, and binding of the antibody to cells in the patient can be evaluated, e.g., by external scanning for radioactivity or by analyzing a biopsy taken from a patient previously exposed to the antibody.

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody, oligopeptide or other organic molecule so as to generate a "labeled" antibody, oligopeptide or other organic molecule. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (e.g., At²¹¹, I¹³¹, I¹²⁵, Y⁹⁰, Re¹⁸⁶, Re¹⁸⁸,

Sm¹⁵³, Bi²¹², P³² and radioactive isotopes of Lu), chemotherapeutic agents e.g. methotrexate, adriamycin, vinca alkaloids (vincristine, vinblastine, etoposide), doxorubicin, melphalan, mitomycin C, chlorambucil, daunorubicin or other intercalating agents, enzymes and fragments thereof such as nucleolytic enzymes, antibiotics, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including fragments and/or variants thereof, and the various antitumor or anticancer agents disclosed below. Other cytotoxic agents are described below. A tumoricidal agent causes destruction of tumor cells.

A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell, especially a TAHO-expressing cancer cell, either in vitro or in vivo. Thus, the growth inhibitory agent may be one which significantly reduces the percentage of TAHO-expressing cells in S phase. Examples of growth inhibitory agents include agents that block cell cycle progression (at a place other than S phase), such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vincas (vincristine and vinblastine), taxanes, and topoisomerase II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in *The Molecular Basis of Cancer*, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogenes, and antineoplastic drugs" by Murakami et al. (WB Saunders: Philadelphia, 1995), especially p. 13. The taxanes (paclitaxel and docetaxel) are anticancer drugs both derived from the yew tree. Docetaxel (TAXOTERE®, Rhone-Poulenc Rorer), derived from the European yew, is a semisynthetic analogue of paclitaxel (TAXOL®, Bristol-Myers Squibb). Paclitaxel and docetaxel promote the assembly of microtubules from tubulin dimers and stabilize microtubules by preventing depolymerization, which results in the inhibition of mitosis in cells.

"Doxorubicin" is an anthracycline antibiotic. The full chemical name of doxorubicin is (8S-cis)-10-[(3-amino-2,3,6-trideoxy- α -L-lyxo-hexapyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione.

The term "cytokine" is a generic term for proteins released by one cell population which act on another cell as intercellular mediators. Examples of such cytokines are lymphokines, monokines, and traditional polypeptide hormones. Included among the cytokines are growth hormone such as human growth hormone, N-methionyl human growth hormone, and bovine growth hormone; parathyroid hormone; thyroxine; insulin; proinsulin; relaxin; prorelaxin; glycoprotein hormones such as follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and luteinizing hormone (LH); hepatic growth factor; fibroblast growth factor; prolactin; placental lactogen; tumor necrosis factor- α and - β ; mullerian-inhibiting substance; mouse gonadotropin-associated peptide; inhibin; activin; vascular endothelial growth factor; integrin; thrombopoietin (TPO); nerve growth factors such as NGF- β ; platelet-growth factor; transforming growth factors (TGFs) such as TGF- α and TGF- β ; insulin-like growth factor-I and -II; erythropoietin (EPO); osteoinductive factors; interferons such as interferon- α , - β , and - γ ; colony stimulat

ing factors (CSFs) such as macrophage-CSF (M-CSF); granulocyte-macrophage-CSF (GM-CSF); and granulocyte-CSF (G-CSF); interleukins (ILs) such as IL-1, IL-1a, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12; a tumor necrosis factor such as TNF- α or TNF- β ; and other polypeptide factors including LIF and kit ligand (KL). As used herein, the term cytokine includes proteins from natural sources or

from recombinant cell culture and biologically active equivalents of the native sequence cytokines.

The term “package insert” is used to refer to instructions customarily included in commercial packages of therapeutic products, that contain information about the indications, usage, dosage, administration, contraindications and/or warnings concerning the use of such therapeutic products.

TABLE 1

```

/*
 *
 * C-C increased from 12 to 15
 * Z is average of EQ
 * B is average of ND
 * match with stop is _M; stop-stop = 0; J (joker) match = 0
 */
#define _M -8 /* value of a match with a stop */
int _day[26][26] = {
/* A B C D E F G H I J K L M N O P Q R S T U V W X Y Z */
/* A */ { 2, 0, -2, 0, 0, -4, 1, -1, -1, 0, -1, -2, -1, 0, _M, 1, 0, -2, 1, 1, 0, 0, -6, 0, -3, 0},
/* B */ { 0, 3, -4, 3, 2, -5, 0, 1, -2, 0, 0, -3, -2, 2, _M, -1, 1, 0, 0, 0, 0, -2, -5, 0, -3, 1},
/* C */ {-2, -4, 15, -5, -5, -4, -3, -3, -2, 0, -5, -6, -5, -4, _M, -3, -5, -4, 0, -2, 0, -2, -8, 0, 0, -5},
/* D */ { 0, 3, -5, 4, 3, -6, 1, 1, -2, 0, 0, -4, -3, 2, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 2},
/* E */ { 0, 2, -5, 3, 4, -5, 0, 1, -2, 0, 0, -3, -2, 1, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 3},
/* F */ {-4, -5, -4, -6, -5, 9, -5, -2, 1, 0, -5, 2, 0, -4, _M, -5, -5, -4, -3, -3, 0, -1, 0, 0, 7, -5},
/* G */ { 1, 0, -3, 1, 0, -5, 5, -2, -3, 0, -2, -4, -3, 0, _M, -1, -1, -3, 1, 0, 0, -1, -7, 0, -5, 0},
/* H */ {-1, 1, -3, 1, 1, -2, -2, 6, -2, 0, 0, -2, -2, 2, _M, 0, 3, 2, -1, -1, 0, -2, -3, 0, 0, 2},
/* I */ {-1, -2, -2, -2, -2, 1, -3, -2, 5, 0, -2, 2, 2, -2, _M, -2, -2, -2, -1, 0, 0, 4, -5, 0, -1, -2},
/* J */ { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* K */ {-1, 0, -5, 0, 0, -5, -2, 0, -2, 0, 5, -3, 0, 1, _M, -1, 1, 3, 0, 0, 0, -2, -3, 0, -4, 0},
/* L */ {-2, -3, -6, -4, -3, 2, -4, -2, 2, 0, -3, 6, 4, -3, _M, -3, -2, -3, -3, -1, 0, 2, -2, 0, -1, -2},
/* M */ {-1, -2, -5, -3, -2, 0, -3, -2, 2, 0, 0, 4, 6, -2, _M, -2, -1, 0, -2, -1, 0, 2, -4, 0, -2, -1},
/* N */ { 0, 2, -4, 2, 1, -4, 0, 2, -2, 0, 1, -3, -2, 2, _M, -1, 1, 0, 1, 0, 0, -2, -4, 0, -2, 1},
/* O */ { _M, 0, _M, _M,
_M, _M, _M, _M, _M, _M, _M, _M, _M},
/* P */ { 1, -1, -3, -1, -1, -5, -1, 0, -2, 0, -1, -3, -2, -1, _M, 6, 0, 0, 1, 0, 0, -1, -6, 0, -5, 0},
/* Q */ { 0, 1, -5, 2, 2, -5, -1, 3, -2, 0, 1, -2, -1, 1, _M, 0, 4, 1, -1, -1, 0, -2, -5, 0, -4, 3},
/* R */ {-2, 0, -4, -1, -1, -4, -3, 2, -2, 0, 3, -3, 0, 0, _M, 0, 1, 6, 0, -1, 0, -2, 2, 0, -4, 0},
/* S */ { 1, 0, 0, 0, 0, -3, 1, -1, -1, 0, 0, -3, -2, 1, _M, 1, -1, 0, 2, 1, 0, -1, -2, 0, -3, 0},
/* T */ { 1, 0, -2, 0, 0, -3, 0, -1, 0, 0, 0, -1, -1, 0, _M, 0, -1, -1, 1, 3, 0, 0, -5, 0, -3, 0},
/* U */ { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* V */ { 0, -2, -2, -2, -2, -1, -1, -2, 4, 0, -2, 2, 2, -2, _M, -1, -2, -2, -1, 0, 0, 4, -6, 0, -2, -2},
/* W */ {-6, -5, -8, -7, -7, 0, -7, -3, -5, 0, -3, -2, -4, -4, _M, -6, -5, 2, -2, -5, 0, -6, 17, 0, 0, -6},
/* X */ { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* Y */ {-3, -3, 0, -4, -4, 7, -5, 0, -1, 0, -4, -1, -2, -2, _M, -5, -4, -4, -3, -3, 0, -2, 0, 0, 10, -4},
/* Z */ { 0, 1, -5, 2, 3, -5, 0, 2, -2, 0, 0, -2, -1, 1, _M, 0, 3, 0, 0, 0, 0, -2, -6, 0, -4, 4}
};
/*
 */
#include <stdio.h>
#include <ctype.h>
#define MAXJMP 16 /* max jumps in a diag */
#define MAXGAP 24 /* don't continue to penalize gaps larger than this */
#define JMPS 1024 /* max jumps in an path */
#define MX 4 /* save if there's at least MX-1 bases since last jmp */
#define DMAT 3 /* value of matching bases */
#define DMIS 0 /* penalty for mismatched bases */
#define DINS0 8 /* penalty for a gap */
#define DINS1 1 /* penalty per base */
#define PINS0 8 /* penalty for a gap */
#define PINS1 4 /* penalty per residue */
struct jmp {
short n[MAXJMP]; /* size of jmp (neg for dely) */
unsigned short x[MAXJMP]; /* base no. of jmp in seq x */
};
struct diag {
int score; /* score at last jmp */
long offset; /* offset of prev block */
short ijmp; /* current jmp index */
struct jmp jp; /* list of jmps */
};
struct path {
int spc; /* number of leading spaces */
short n[JMPS]; /* size of jmp (gap) */
int x[JMPS]; /* loc of jmp (last elem before gap) */
};
char *ofile; /* output file name */
char *namex[2]; /* seq names: getseqs() */
char *prog; /* prog name for err msgs */

```

TABLE 1-continued

```

char          *seqx[2];          /* seqs: getseqs( ) */
int           dmax;              /* best diag: nw( ) */
int           dmax0;             /* final diag */
int           dna;               /* set if dna: main( ) */
int           endgaps;           /* set if penalizing end gaps */
int           gapx, gapy;        /* total gaps in seqs */
int           len0, len1;        /* seq lens */
int           ngapx, ngapy;      /* total size of gaps */
int           smax;              /* max score: nw( ) */
int           *xbm;              /* bitmap for matching */
long          offset;           /* current offset in jmp file */
struct        diag               *dx;          /* holds diagonals */
struct        path               pp[2];       /* holds path for seqs */
char          *calloc( ), *malloc( ), *index( ), *strcpy( );
char          *getseq( ), *g_calloc( );
/* Needleman-Wunsch alignment program
*
* usage: progs file1 file2
* where file1 and file2 are two dna or two protein sequences.
* The sequences can be in upper- or lower-case and may contain ambiguity
* Any lines beginning with ';', '>' or '<' are ignored
* Max file length is 65535 (limited by unsigned short x in the jmp struct)
* A sequence with 1/3 or more of its elements ACGTU is assumed to be DNA
* Output is in the file "align.out"
*
* The program may create a tmp file in /tmp to hold info about traceback.
* Original version developed under BSD 4.3 on a vax 8650
*/
#include "nw.h"
#include "day.h"
static        _dbval[26] = {
                1,14,2,13,0,0,4,11,0,0,12,0,3,15,0,0,0,5,6,8,8,7,9,0,10,0
};
static        _pbval[26] = {
                1, 2((1<<('D'-'A'))|(1<<('N'-'A'))), 4, 8, 16, 32, 64,
                128, 256, 0xFFFFFFFF, 1<<10, 1<<11, 1<<12, 1<<13, 1<<14,
                1<<15, 1<<16, 1<<17, 1<<18, 1<<19, 1<<20, 1<<21, 1<<22,
                1<<23, 1<<24, 1<<25((1<<('E'-'A'))|(1<<('Q'-'A')))
};
main(ac, av)                                     main
{
    int         ac;
    char        *av[ ];
    {
        prog = av[0];
        if(ac != 3) {
            fprintf(stderr, "usage: %s file1 file2\n", prog);
            fprintf(stderr, "where file1 and file2 are two dna or two protein sequences.\n");
            fprintf(stderr, "The sequences can be in upper- or lower-case\n");
            fprintf(stderr, "Any lines beginning with ';', '>' or '<' are ignored\n");
            fprintf(stderr, "Output is in the file \"align.out\"\n");
            exit(1);
        }
        namex[0] = av[1];
        namex[1] = av[2];
        seqx[0] = getseq(namex[0], &len0);
        seqx[1] = getseq(namex[1], &len1);
        xbm = (dna)? _dbval : _pbval;
        endgaps = 0;          /* 1 to penalize endgaps */
        ofile = "align.out"; /* output file */
        nw( );               /* fill in the matrix, get the possible jmps */
        readjmps( );         /* get the actual jmps */
        print( );           /* print stats, alignment */
        cleanup(0);         /* unlink any tmp files */
    }
}
/* do the alignment, return best score: main( )
* dna: values in Fitch and Smith, PNAS, 80, 1382-1386, 1983
* pro: PAM 250 values
* When scores are equal, we prefer mismatches to any gap, prefer
* a new gap to extending an ongoing gap, and prefer a gap in seqx
* to a gap in seq y.
*/
nw( )
{
    char        *px, *py;      /* seqs and ptrs */
    int         *ndely, *dely; /* keep track of dely */
    int         ndelx, delx;   /* keep track of delx */
    int         *tmp;          /* for swapping row0, row1 */
    int         mis;           /* score for each type */
    int         ins0, ins1;    /* insertion penalties */
    register    id;           /* diagonal index */

```

TABLE 1-continued

```

register    ij;                /* jmp index*/
register    *col0, *col1;      /* score for curr, last row */
register    xx, yy;           /* index into seqs */
dx = (struct diag *)g_calloc("to get diags", len0+len1+1, sizeof(struct diag));
ndely = (int *)g_calloc("to get ndely", len1+1, sizeof(int));
dely = (int *)g_calloc("to get dely", len1+1, sizeof(int));
col0 = (int *)g_calloc("to get col0", len1+1, sizeof(int));
col1 = (int *)g_calloc("to get col1", len1+1, sizeof(int));
ins0 = (dna)? DINS0 : PINS0;
ins1 = (dna)? DINS1 : PINS1;
smax = -10000;
if (endgaps) {
    for (col0[0] = dely[0] = -ins0, yy = 1; yy <= len1; yy++) {
        col0[yy] = dely[yy] = col0[yy-1] - ins1;
        ndely[yy] = yy;
    }
    col0[0] = 0;          /* Waterman Bull Math Biol 84 */
}
else
    for (yy = 1; yy <= len1; yy++)
        dely[yy] = -ins0;
/* fill in match matrix
*/
for (px = seqx[0], xx = 1; xx <= len0; px++, xx++) {
    /* initialize first entry in col
    */
    if (endgaps) {
        if (xx == 1)
            col1[0] = delx = -(ins0+ins1);
        else
            col1[0] = delx = col0[0] - ins1;
        ndelx = xx;
    }
    else {
        col1[0] = 0;
        delx = -ins0;
        ndelx = 0;
    }
}

...nw
for (py = seqx[1], yy = 1; yy <= len1; py++, yy++) {
    mis = col0[yy-1];
    if (dna)
        mis += (xbm[*px-'A']&xbm[*py-'A'])? DMAT : DMIS;
    else
        mis += _day[*px-'A'][*py-'A'];
    /* update penalty for del in x seq;
    * favor new del over ongong del
    * ignore MAXGAP if weighting endgaps
    */
    if (endgaps || ndely[yy] < MAXGAP) {
        if (col0[yy] - ins0 >= dely[yy]) {
            dely[yy] = col0[yy] - (ins0+ins1);
            ndely[yy] = 1;
        }
        else {
            dely[yy] -= ins1;
            ndely[yy]++;
        }
    }
    else {
        if (col0[yy] - (ins0+ins1) >= dely[yy]) {
            dely[yy] = col0[yy] - (ins0+ins1);
            ndely[yy] = 1;
        }
        else
            ndely[yy]++;
    }
    /* update penalty for del in y seq;
    * favor new del over ongong del
    */
    if (endgaps || ndelx < MAXGAP) {
        if (col1[yy-1] - ins0 >= delx) {
            delx = col1[yy-1] - (ins0+ins1);
            ndelx = 1;
        }
        else {
            delx -= ins1;
            ndelx++;
        }
    }
    else {
        if (col1[yy-1] - (ins0+ins1) >= delx) {
            delx = col1[yy-1] - (ins0+ins1);
            ndelx = 1;
        }
        else
    }
}

```

TABLE 1-continued

```

        ndelx++;
    }
    /* pick the maximum score; we're favoring
    * mis over any del and delx over dely
    */

    id = xx - yy + len1 - 1;
    if (mis >= delx && mis >= dely[yy])
        col1[yy] = mis;
    else if (delx >= dely[yy]) {
        col1[yy] = delx;
        ij = dx[id].ijmp;
        if (dx[id].jp.n[0] &&& (!dna || (ndelx >= MAXJMP
        && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
            dx[id].ijmp++;
            if (++ij >= MAXJMP) {
                writeimps(id);
                ij = dx[id].ijmp = 0;
                dx[id].offset = offset;
                offset += sizeof(struct jmp) + sizeof(offset);
            }
        }
        dx[id].jp.n[ij] = ndelx;
        dx[id].jp.x[ij] = xx;
        dx[id].score = delx;
    }
    else {
        col1[yy] = dely[yy];
        ij = dx[id].ijmp;
        if (dx[id].jp.n[0] &&& (!dna || (ndely[yy] >= MAXJMP
        && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
            dx[id].ijmp++;
            if (++ij >= MAXJMP) {
                writeimps(id);
                ij = dx[id].ijmp = 0;
                dx[id].offset = offset;
                offset += sizeof(struct jmp) + sizeof(offset);
            }
        }
        dx[id].jp.n[ij] = -ndely[yy];
        dx[id].jp.x[ij] = xx;
        dx[id].score = dely[yy];
    }
    if (xx == len0 && yy < len1) {
        /* last col
        */
        if (endgaps)
            col1[yy] -= ins0+ins1*(len1-yy);
        if (col1[yy] > smax) {
            smax = col1[yy];
            dmax = id;
        }
    }
    if (endgaps && xx < len0)
        col1[yy-1] -= ins0+ins1*(len0-xx);
    if (col1[yy-1] > smax) {
        smax = col1[yy-1];
        dmax = id;
    }
    tmp = col0; col0 = col1; col1 = tmp;
}
(void) free((char *)ndely);
(void) free((char *)dely);
(void) free((char *)col0);
(void) free((char *)col1);
}
/*
*
* print() -- only routine visible outside this module
*
* static:
* getmat() -- trace back best path, count matches: print()
* pr_align() -- print alignment of described in array p[ ]: print()
* dumpblock() -- dump a block of lines with numbers, stars: pr_align()
* nums() -- put out a number line: dumpblock()
* putline() -- put out a line (name, [num], seq, [num]): dumpblock()
* stars() -- put a line of stars: dumpblock()
* stripname() -- strip any path and prefix from a seqname
*/
#include "nw.h"
#define SPC 3

```

TABLE 1-continued

```

#define P_LINE      256      /* maximum output line */
#define P_SPC       3        /* space between name or num and seq */
extern      _day[26][26];
int         olen;          /* set output line length */
FILE        *fx;          /* output file */
print()
{
    int      lx, ly, firstgap, lastgap;      /* overlap */
    if ((fx = fopen(ofile, "w")) == 0) {
        fprintf(stderr, "%s: can't write %s\n", prog, ofile);
        cleanup(1);
    }
    fprintf(fx, "<first sequence: %s (length = %d)\n", namex[0], len0);
    fprintf(fx, "<second sequence: %s (length = %d)\n", namex[1], len1);
    olen = 60;
    lx = len0;
    ly = len1;
    firstgap = lastgap = 0;
    if (dmax < len1 - 1) {          /* leading gap in x */
        pp[0].spc = firstgap = len1 - dmax - 1;
        ly -= pp[0].spc;
    }
    else if (dmax > len1 - 1) {     /* leading gap in y */
        pp[1].spc = firstgap = dmax - (len1 - 1);
        lx -= pp[1].spc;
    }
    if (dmax0 < len0 - 1) {        /* trailing gap in x */
        lastgap = len0 - dmax0 - 1;
        lx -= lastgap;
    }
    else if (dmax0 > len0 - 1) {   /* trailing gap in y */
        lastgap = dmax0 - (len0 - 1);
        ly -= lastgap;
    }
    getmat(lx, ly, firstgap, lastgap);
    pr_align();
}
/*
 * trace back the best path, count matches
 */
static
getmat(lx, ly, firstgap, lastgap)          getmat
    int      lx, ly;          /* "core" (minus endgaps) */
    int      firstgap, lastgap;      /* leading trailing overlap */
{
    int      nm, i0, i1, siz0, siz1;
    char     outx[32];
    double   pct;
    register n0, n1;
    register char *p0, *p1;
    /* get total matches, score
     */
    i0 = i1 = siz0 = siz1 = 0;
    p0 = seqx[0] + pp[1].spc;
    p1 = seqx[1] + pp[0].spc;
    n0 = pp[1].spc + 1;
    n1 = pp[0].spc + 1;
    nm = 0;
    while (*p0 && *p1) {
        if (siz0) {
            p1++;
            n1++;
            siz0--;
        }
        else if (siz1) {
            p0++;
            n0++;
            siz1--;
        }
        else {
            if (xbm[*p0-'A'] & xbm[*p1-'A'])
                nm++;
            if (n0++ == pp[0].x[i0])
                siz0 = pp[0].n[i0++];
            if (n1++ == pp[1].x[i1])
                siz1 = pp[1].n[i1++];
            p0++;
            p1++;
        }
    }
}
/* pct homology:

```

TABLE 1-continued

```

* if penalizing endgaps, base is the shorter seq
* else, knock off overhangs and take shorter core
*/
if (endgaps)
    lx = (len0 < len1)? len0 : len1;
else
    lx = (lx < ly)? lx : ly;
pct = 100.*(double)nm/(double)lx;
fprintf(fx, "\n");
fprintf(fx, "<<%d match %s in an overlap of %d: %.2f percent similarity\n",
        nm, (nm == 1)? "" : "es", lx, pct);
fprintf(fx, "<<gaps in first sequence: %d", gapx);
if (gapx) {
    (void) sprintf(outx, "(%d %s%s)",
        ngapx, (dna)? "base":"residue", (ngapx == 1)? "" : "s");
    fprintf(fx, "%s", outx);
}
fprintf(fx, " gaps in second sequence: %d", gapy);
if (gapy) {
    (void) sprintf(outx, "(%d %s%s)",
        ngapy, (dna)? "base":"residue", (ngapy == 1)? "" : "s");
    fprintf(fx, "%s", outx);
}
}
if (dna)
    fprintf(fx,
        "\n<score: %d (match = %d, mismatch = %d, gap penalty = %d + %d per base)\n",
        smax, DMAT, DMIS, DINS0, DINS1);
else
    fprintf(fx,
        "\n<score: %d (Dayhoff PAM 250 matrix, gap penalty = %d + %d per residue)\n",
        smax, PINS0, PINS1);
if (endgaps)
    fprintf(fx,
        "<<endgaps penalized. left endgap: %d %s%s, right endgap: %d %s%s\n",
        firstgap, (dna)? "base" : "residue", (firstgap == 1)? "" : "s",
        lastgap, (dna)? "base" : "residue", (lastgap == 1)? "" : "s");
else
    fprintf(fx, "<<endgaps not penalized\n");
}
static      nm;          /* matches in core -- for checking */
static      lmax;       /* lengths of stripped file names */
static      ij[2];      /* jmp index for a path */
static      nc[2];      /* number at start of current line */
static      ni[2];      /* current elem number -- for gapping */
static      siz[2];
static char *ps[2];     /* ptr to current element */
static char *po[2];     /* ptr to next output char slot */
static char out[2][P_LINE]; /* output line */
static char star[P_LINE]; /* set by stars() */
/*
* print alignment of described in struct path pp[ ]
*/
static
pr_align( )
{
    int      nn;        /* char count */
    int      more;
    register i;
    for (i = 0, lmax = 0; i < 2; i++) {
        nn = stripname(name[i]);
        if (nn > lmax)
            lmax = nn;
        nc[i] = 1;
        ni[i] = 1;
        siz[i] = ij[i] = 0;
        ps[i] = seq[i];
        po[i] = out[i];
    }
    for (nn = nm = 0, more = 1; more;) {
        for (i = more = 0; i < 2; i++) {
            /*
             * do we have more of this sequence?
             */
            if (!*ps[i])
                continue;
            more++;
            if (pp[i].spc) { /* leading space */
                *po[i]++ = ' ';
                pp[i].spc--;
            }
            else if (siz[i]) { /* in a gap */
                *po[i]++ = '-';
            }
        }
        /*
         * print alignment of described in struct path pp[ ]
         */
        pr_align( )
    }
}

```

...getmat

pr_align

...pr_align

TABLE 1-continued

```

        siz[i]--;
    }
    else {
        /* we're putting a seq element
        */
        *po[i] = *ps[i];
        if (islower(*ps[i]))
            *ps[i] = toupper(*ps[i]);
        po[i]++;
        ps[i]++;
        /*
        * are we at next gap for this seq?
        */
        if (ni[i] == pp[i].x[ij[i]]) {
            /*
            * we need to merge all gaps
            * at this location
            */
            siz[i] = pp[i].n[ij[i]++];
            while (ni[i] == pp[i].x[ij[i]])
                siz[i] += pp[i].n[ij[i]++];
        }
        ni[i]++;
    }
}
if (++nn == olen || !more && nn) {
    dumpblock();
    for (i = 0; i < 2; i++)
        po[i] = out[i];
    nn = 0;
}
}
}
/*
* dump a block of lines, including numbers, stars: pr_align()
*/
static
dumpblock()
{
    register i;
    for (i = 0; i < 2; i++)
        *po[i]-- = '\0';

    (void) puts("\n", fx);
    for (i = 0; i < 2; i++) {
        if (*out[i] && (*out[i] != ' ' || *(po[i]) != ' ')) {
            if (i == 0)
                nums(i);
            if (i == 0 && *out[1])
                stars();
            putline(i);
            if (i == 0 && *out[1])
                fprintf(fx, star);
            if (i == 1)
                nums(i);
        }
    }
}
/*
* put out a number line: dumpblock()
*/
static
nums(ix)
int ix; /* index in out[] holding seq line */
{
    char nline[P_LINE];
    register i, j;
    register char *pn, *px, *py;
    for (pn = nline, i = 0; i < lmax+P_SPC; i++, pn++)
        *pn = ' ';
    for (i = nc[ix], py = out[ix]; *py; py++, pn++) {
        if (*py == ' ' || *py == '-')
            *pn = ' ';
        else {
            if (i%10 == 0 || (i == 1 && nc[ix] != 1)) {
                j = (i < 0)? -i : i;
                for (px = pn; j; j /= 10, px--)
                    *px = j%10 + '0';
                if (i < 0)
                    *px = '-';
            }
        }
    }
}

```

dumpblock

...dumpblock

nums

TABLE 1-continued

```

        else
            *pn = ' ';
            i++;
        }
    }
    *pn = '\0';
    nc[ix] = i;
    for (pn = nline; *pn; pn++)
        (void) putc(*pn, fx);
    (void) putc('\n', fx);
}
/*
 * put out a line (name, [num], seq, [num]): dumpblock()
 */
static
putline(ix)                                putline
{
    int ix;                                  ...putline

    int i;
    register char *px;
    for (px = name[ix], i = 0; *px && *px != ' '; px++, i++)
        (void) putc(*px, fx);
    for (; i < lmax+P_SPC; i++)
        (void) putc(' ', fx);
    /* these count from 1:
     * ni[ ] is current element (from 1)
     * nc[ ] is number at start of current line
     */
    for (px = out[ix]; *px; px++)
        (void) putc(*px&0x7F, fx);
    (void) putc('\n', fx);
}
/*
 * put a line of stars (seqs always in out[0], out[1]): dumpblock()
 */
static
stars()                                    stars
{
    int i;
    register char *p0, *p1, cx, *px;
    if (!*out[0] || (*out[0] == ' ' && *(p0[0]) == ' ') ||
        !*out[1] || (*out[1] == ' ' && *(p0[1]) == ' '))
        return;
    px = star;
    for (i = lmax+P_SPC; i; i--)
        *px++ = ' ';
    for (p0 = out[0], p1 = out[1]; *p0 && *p1; p0++, p1++) {
        if (isalpha(*p0) && isalpha(*p1)) {
            if (xbm[*p0-'A']&xbm[*p1-'A']) {
                cx = '*';
                nm++;
            }
            else if (!dna && _day[*p0-'A'][*p1-'A'] > 0)
                cx = '.';
            else
                cx = ' ';
        }
        else
            cx = ' ';
        *px++ = cx;
    }
    *px++ = '\n';
    *px = '\0';
}
/*
 * strip path or prefix from pn, return len: pr_align()
 */
static
stripname(pn)                              stripname
{
    char *pn; /* file name (may be path) */

    register char *px, *py;
    py = 0;
    for (px = pn; *px; px++)
        if (*px == '/')
            py = px + 1;
    if (py)
        (void) strcpy(pn, py);
    return(strlen(pn));
}

```

TABLE 1-continued

```

/*
 * cleanup() -- cleanup any tmp file
 * getseq() -- read in seq, set dna, len, maxlen
 * g_alloc() -- calloc() with error checkin
 * readjimps() -- get the good jimps, from tmp file if necessary
 * writejimps() -- write a filled array of jimps to a tmp file: nw()
 */
#include "nw.h"
#include <sys/file.h>
char      *jname = "/tmp/homgXXXXXX";      /* tmp file for jimps */
FILE      *fj;
int        cleanup();                      /* cleanup tmp file */
long      lseek();
/*
 * remove any tmp file if we blow
 */
cleanup(i)                                  cleanup
{
    int i;
    {
        if (fj)
            (void) unlink(jname);
        exit(i);
    }
}
/*
 * read, return ptr to seq, set dna, len, maxlen
 * skip lines starting with ';', '<', or '>'
 * seq in upper or lower case
 */
char      *
getseq(file, len)                          getseq
{
    char      *file; /* file name */
    int        *len; /* seq len */
    {
        char      line[1024], *pseq;
        register char *px, *py;
        int        natgc, tlen;
        FILE      *fp;
        if ((fp = fopen(file, "r")) == 0) {
            fprintf(stderr, "%s: can't read %s\n", prog, file);
            exit(1);
        }
        tlen = natgc = 0;
        while (fgets(line, 1024, fp)) {
            if (*line == ';' || *line == '<' || *line == '>')
                continue;
            for (px = line; *px != '\n'; px++)
                if (isupper(*px) || islower(*px))
                    tlen++;
        }
        if ((pseq = malloc((unsigned)(tlen+6))) == 0) {
            fprintf(stderr, "%s: malloc( ) failed to get %d bytes for %s\n", prog, tlen+6, file);
            exit(1);
        }
        pseq[0] = pseq[1] = pseq[2] = pseq[3] = '\0';
        py = pseq + 4;
        *len = tlen;
        rewind(fp);
        while (fgets(line, 1024, fp)) {
            if (*line == ';' || *line == '<' || *line == '>')
                continue;
            for (px = line; *px != '\n'; px++) {
                if (isupper(*px))
                    *py++ = *px;
                else if (islower(*px))
                    *py++ = toupper(*px);
                if (index("ATGCU", *(py-1)))
                    natgc++;
            }
        }
        *py++ = '\0';
        *py = '\0';
        (void) fclose(fp);
        dna = natgc > (tlen/3);
        return(pseq+4);
    }
}
char      *
g_alloc(msg, nx, sz)                        g_alloc
{
    char      *msg; /* program, calling routine */
    int        nx, sz; /* number and size of elements */

```

TABLE 1-continued

```

{
    char          *px, *calloc();
    if ((px = calloc((unsigned)nx, (unsigned)sz)) == 0) {
        if (*msg) {
            fprintf(stderr, "%s: g_calloc() failed %s (n=%d, sz=%d)\n", prog, msg, nx, sz);
            exit(1);
        }
    }
    return(px);
}
/*
* get final jmps from dx[ ] or tmp file, set pp[ ], reset dmax: main()
*/
readjmps()                                     readjmps
{
    int          fd = -1;
    int          siz, i0, i1;
    register i, j, xx;
    if (fj) {
        (void) fclose(fj);
        if ((fd = open(jname, O_RDONLY, 0)) < 0) {
            fprintf(stderr, "%s: can't open( ) %s\n", prog, jname);
            cleanup(1);
        }
    }
    for (i = i0 = i1 = 0, dmax0 = dmax, xx = len0; ; i++) {
        while (1) {
            for (j = dx[dmax].ijmp; j >= 0 && dx[dmax].jp.x[j] >= xx; j--)
                ;
            if (j < 0 && dx[dmax].offset && fj) {
                (void) lseek(fd, dx[dmax].offset, 0);
                (void) read(fd, (char *)&dx[dmax].jp, sizeof(struct jmp));
                (void) read(fd, (char *)&dx[dmax].offset, sizeof(dx[dmax].offset));
                dx[dmax].ijmp = MAXJMP-1;
            }
            else
                break;
        }
        if (i >= JMPS) {
            fprintf(stderr, "%s: too many gaps in alignment\n", prog);
            cleanup(1);
        }
        if (j >= 0) {
            siz = dx[dmax].jp.n[j];
            xx = dx[dmax].jp.x[j];
            dmax += siz;
            if (siz < 0) {
                /* gap in second seq */
                pp[1].n[i1] = -siz;
                xx += siz;
                /* id = xx - yy + len1 - 1 */
                pp[1].x[i1] = xx - dmax + len1 - 1;
                gapy++;
                ngapy -= siz;
            }
            /* ignore MAXGAP when doing endgaps */
            siz = (-siz < MAXGAP || endgaps)? -siz : MAXGAP;
            i1++;
        }
        else if (siz > 0) {
            /* gap in first seq */
            pp[0].n[i0] = siz;
            pp[0].x[i0] = xx;
            gapx++;
            ngapx += siz;
        }
        /* ignore MAXGAP when doing endgaps */
        siz = (siz < MAXGAP || endgaps)? siz : MAXGAP;
        i0++;
    }
    else
        break;
}
/* reverse the order of jmps */
for (j = 0, i0--, j < i0; j++, i0--) {
    i = pp[0].n[j]; pp[0].n[j] = pp[0].n[i0]; pp[0].n[i0] = i;
    i = pp[0].x[j]; pp[0].x[j] = pp[0].x[i0]; pp[0].x[i0] = i;
}
for (j = 0, i1--, j < i1; j++, i1--) {
    i = pp[1].n[j]; pp[1].n[j] = pp[1].n[i1]; pp[1].n[i1] = i;
    i = pp[1].x[j]; pp[1].x[j] = pp[1].x[i1]; pp[1].x[i1] = i;
}
if (fd >= 0)
    (void) close(fd);

```

TABLE 1-continued

```

if (fj) {
    (void) unlink(jname);
    fj = 0;
    offset = 0;
}
}
/*
 * write a filled jmp struct offset of the prev one (if any): nw( )
 */
writejumps(ix)
int ix;
{
    char *mktemp( );
    if (!fj) {
        if (mktemp(jname) < 0) {
            fprintf(stderr, "%s: can't mktemp( ) %s\n", prog, jname);
            cleanup(1);
        }
        if ((fj = fopen(jname, "w")) == 0) {
            fprintf(stderr, "%s: can't write %s\n", prog, jname);
            exit(1);
        }
    }
    (void) fwrite((char *)&dx[ix].jp, sizeof(struct jmp), 1, fj);
    (void) fwrite((char *)&dx[ix].offset, sizeof(dx[ix].offset), 1, fj);
}

```

TABLE 2

TAHO	XXXXXXXXXXXXXXXX	(Length = 15 amino acids)
Comparison Protein	XXXXXXXXYYYYYYY	(Length = 12 amino acids)

% amino acid sequence identity = (the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the TAHO polypeptide) = 5 divided by 15 = 33.3%

TABLE 3

TAHO	XXXXXXXXXX	(Length = 10 amino acids)
Comparison Protein	XXXXXXXXYYYYZZYZ	(Length = 15 amino acids)

% amino acid sequence identity = (the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the TAHO polypeptide) = 5 divided by 10 = 50%

TABLE 4

TAHO-DNA	NNNNNNNNNNNN	(Length = 14 nucleotides)
Comparison DNA	NNNNNNLLLLLLLL	(Length = 16 nucleotides)

% nucleic acid sequence identity = (the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the TAHO-DNA nucleic acid sequence) = 6 divided by 14 = 42.9%

TABLE 5

TAHO-DNA	NNNNNNNNNN	(Length = 12 nucleotides)
Comparison DNA	NNNNLLVV	(Length = 9 nucleotides)

% nucleic acid sequence identity = (the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the TAHO-DNA nucleic acid sequence) = 4 divided by 12 = 33.3%

II. Compositions and Methods of the Invention

A. Anti-TAHO Antibodies

In one embodiment, the present invention provides anti-TAHO antibodies which may find use herein as therapeutic agents. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

25 1. Polyclonal Antibodies

Polyclonal antibodies are preferably raised in animals by multiple subcutaneous (sc) or intraperitoneal (ip) injections of the relevant antigen and an adjuvant. It may be useful to conjugate the relevant antigen (especially when synthetic peptides are used) to a protein that is immunogenic in the species to be immunized. For example, the antigen can be conjugated to keyhole limpet hemocyanin (KLH), serum albumin, bovine thyroglobulin, or soybean trypsin inhibitor, using a bifunctional or derivatizing agent, e.g., maleimido-benzoyl sulfosuccinimide ester (conjugation through cysteine residues), N-hydroxysuccinimide (through lysine residues), glutaraldehyde, succinic anhydride, SOCl₂, or R¹N=C=NR, where R and R¹ are different alkyl groups.

30 40 Animals are immunized against the antigen, immunogenic conjugates, or derivatives by combining, e.g., 100 µg or 5.1 µg of the protein or conjugate (for rabbits or mice, respectively) with 3 volumes of Freund's complete adjuvant and injecting the solution intradermally at multiple sites. One month later, the animals are boosted with 1/5 to 1/10 the original amount of peptide or conjugate in Freund's complete adjuvant by subcutaneous injection at multiple sites. Seven to 14 days later, the animals are bled and the serum is assayed for antibody titer. Animals are boosted until the titer plateaus. Conjugates also can be made in recombinant cell culture as protein fusions. Also, aggregating agents such as alum are suitably used to enhance the immune response.

2. Monoclonal Antibodies

Monoclonal antibodies may be made using the hybridoma method first described by Kohler et al., *Nature*, 256:495 (1975), or may be made by recombinant DNA methods (U.S. Pat. No. 4,816,567).

In the hybridoma method, a mouse or other appropriate host animal, such as a hamster, is immunized as described above to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the protein used for immunization. Alternatively, lymphocytes may be immunized in vitro. After immunization, lymphocytes are isolated and then fused with a myeloma cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, *Monoclonal Antibodies: Principles and Practice*, pp. 59-103 (Academic Press, 1986)).

The hybridoma cells thus prepared are seeded and grown in a suitable culture medium which medium preferably contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells (also referred to as fusion partner). For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the selective culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

Preferred fusion partner myeloma cells are those that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive to a selective medium that selects against the unfused parental cells. Preferred myeloma cell lines are murine myeloma lines, such as those derived from MOPC-21 and MPC-11 mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, Calif. USA, and SP-2 and derivatives e.g., X63-Ag8-653 cells available from the American Type Culture Collection, Manassas, Va., USA. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, *J. Immunol.*, 133:3001 (1984); and Brodeur et al., *Monoclonal Antibody Production Techniques and Applications*, pp. 51-63 (Marcel Dekker, Inc., New York, 1987)).

Culture medium in which hybridoma cells are growing is assayed for production of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunosorbent assay (ELISA).

The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis described in Munson et al., *Anal. Biochem.*, 107:220 (1980).

Once hybridoma cells that produce antibodies of the desired specificity, affinity, and/or activity are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods (Goding, *Monoclonal Antibodies: Principles and Practice*, pp. 59-103 (Academic Press, 1986)). Suitable culture media for this purpose include, for example, D-MEM or RPMI-1640 medium. In addition, the hybridoma cells may be grown in vivo as ascites tumors in an animal e.g., by i.p. injection of the cells into mice.

The monoclonal antibodies secreted by the subclones are suitably separated from the culture medium, ascites fluid, or serum by conventional antibody purification procedures such as, for example, affinity chromatography (e.g., using protein A or protein G-Sepharose) or ion-exchange chromatography, hydroxylapatite chromatography, gel electrophoresis, dialysis, etc.

DNA encoding the monoclonal antibodies is readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as *E. coli* cells, simian COS cells, Chinese Hamster Ovary (CHO) cells, or myeloma cells that do not otherwise produce antibody protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. Review articles on recombinant expression in bacteria of DNA encoding the antibody include Skerra et al., *Curr. Opinion in Immunol.*, 5:256-262 (1993) and Plückerthun, *Immunol. Revs.* 130: 151-188 (1992).

In a further embodiment, monoclonal antibodies or antibody fragments can be isolated from antibody phage libraries generated using the techniques described in McCafferty et al., *Nature*, 348:552-554 (1990). Clackson et al., *Nature*, 352: 624-628 (1991) and Marks et al., *J. Mol. Biol.*, 222:581-597 (1991) describe the isolation of murine and human antibodies, respectively, using phage libraries. Subsequent publications describe the production of high affinity (nM range) human antibodies by chain shuffling (Marks et al., *Bio/Technology*, 10:779-783 (1992)), as well as combinatorial infection and in vivo recombination as a strategy for constructing very large phage libraries (Waterhouse et al., *Nuc. Acids. Res.* 21:2265-2266 (1993)). Thus, these techniques are viable alternatives to traditional monoclonal antibody hybridoma techniques for isolation of monoclonal antibodies.

The DNA that encodes the antibody may be modified to produce chimeric or fusion antibody polypeptides, for example, by substituting human heavy chain and light chain constant domain (C_H and C_L) sequences for the homologous murine sequences (U.S. Pat. No. 4,816,567; and Morrison, et al., *Proc. Natl. Acad. Sci. USA*, 81:6851 (1984)), or by fusing the immunoglobulin coding sequence with all or part of the coding sequence for a non-immunoglobulin polypeptide (heterologous polypeptide). The non-immunoglobulin polypeptide sequences can substitute for the constant domains of an antibody, or they are substituted for the variable domains of one antigen-combining site of an antibody to create a chimeric bivalent antibody comprising one antigen-combining site having specificity for an antigen and another antigen-combining site having specificity for a different antigen.

3. Human and Humanized Antibodies

The anti-TAHO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., *Nature*, 321:522-525 (1986); Riech-

mann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Pat. No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

The choice of human variable domains, both light and heavy, to be used in making the humanized antibodies is very important to reduce antigenicity and HAMA response (human anti-mouse antibody) when the antibody is intended for human therapeutic use. According to the so-called "best-fit" method, the sequence of the variable domain of a rodent antibody is screened against the entire library of known human variable domain sequences. The human V domain sequence which is closest to that of the rodent is identified and the human framework region (FR) within it accepted for the humanized antibody (Sims et al., *J. Immunol.* 151:2296 (1993); Chothia et al., *J. Mol. Biol.*, 196:901 (1987)). Another method uses a particular framework region derived from the consensus sequence of all human antibodies of a particular subgroup of light or heavy chains. The same framework may be used for several different humanized antibodies (Carter et al., *Proc. Natl. Acad. Sci. USA*, 89:4285 (1992); Presta et al., *J. Immunol.* 151:2623 (1993)).

It is further important that antibodies be humanized with retention of high binding affinity for the antigen and other favorable biological properties. To achieve this goal, according to a preferred method, humanized antibodies are prepared by a process of analysis of the parental sequences and various conceptual humanized products using three-dimensional models of the parental and humanized sequences. Three-dimensional immunoglobulin models are commonly available and are familiar to those skilled in the art. Computer programs are available which illustrate and display probable three-dimensional conformational structures of selected candidate immunoglobulin sequences. Inspection of these displays permits analysis of the likely role of the residues in the functioning of the candidate immunoglobulin sequence, i.e., the analysis of residues that influence the ability of the candidate immunoglobulin to bind its antigen. In this way, FR residues can be selected and combined from the recipient and import sequences so that the desired antibody characteristic, such as increased affinity for the target antigen(s), is achieved. In general, the hypervariable region residues are directly and most substantially involved in influencing antigen binding.

Various forms of a humanized anti-TAHO antibody are contemplated. For example, the humanized antibody may be an antibody fragment, such as a Fab, which is optionally conjugated with one or more cytotoxic agent(s) in order to generate an immunoconjugate. Alternatively, the humanized antibody may be an intact antibody, such as an intact IgG1 antibody.

As an alternative to humanization, human antibodies can be generated. For example, it is now possible to produce transgenic animals (e.g., mice) that are capable, upon immunization, of producing a full repertoire of human antibodies in the absence of endogenous immunoglobulin production. For example, it has been described that the homozygous deletion of the antibody heavy-chain joining region (J_H) gene in chimeric and germ-line mutant mice results in complete inhibition of endogenous antibody production. Transfer of the human germ-line immunoglobulin gene array into such

germ-line mutant mice will result in the production of human antibodies upon antigen challenge. See, e.g., Jakobovits et al., *Proc. Natl. Acad. Sci. USA*, 90:2551 (1993); Jakobovits et al., *Nature*, 362:255-258 (1993); Bruggemann et al., *Year in Immuno.* 7:33 (1993); U.S. Pat. Nos. 5,545,806, 5,569,825, 5,591,669 (all of GenPharm); 5,545,807; and WO 97/17852.

Alternatively, phage display technology (McCafferty et al., *Nature* 348:552-553 [1990]) can be used to produce human antibodies and antibody fragments in vitro, from immunoglobulin variable (V) domain gene repertoires from unimmunized donors. According to this technique, antibody V domain genes are cloned in-frame into either a major or minor coat protein gene of a filamentous bacteriophage, such as M13 or fd, and displayed as functional antibody fragments on the surface of the phage particle. Because the filamentous particle contains a single-stranded DNA copy of the phage genome, selections based on the functional properties of the antibody also result in selection of the gene encoding the antibody exhibiting those properties. Thus, the phage mimics some of the properties of the B-cell. Phage display can be performed in a variety of formats, reviewed in, e.g., Johnson, Kevin S. and Chiswell, David J., *Current Opinion in Structural Biology* 3:564-571 (1993). Several sources of V-gene segments can be used for phage display. Clackson et al., *Nature*, 352:624-628 (1991) isolated a diverse array of anti-oxazolone antibodies from a small random combinatorial library of V genes derived from the spleens of immunized mice. A repertoire of V genes from unimmunized human donors can be constructed and antibodies to a diverse array of antigens (including self-antigens) can be isolated essentially following the techniques described by Marks et al., *J. Mol. Biol.* 222:581-597 (1991), or Griffith et al., *EMBO J.* 12:725-734 (1993). See, also, U.S. Pat. Nos. 5,565,332 and 5,573,905.

As discussed above, human antibodies may also be generated by in vitro activated B cells (see U.S. Pat. Nos. 5,567,610 and 5,229,275).

4. Antibody fragments

In certain circumstances there are advantages of using antibody fragments, rather than whole antibodies. The smaller size of the fragments allows for rapid clearance, and may lead to improved access to solid tumors.

Various techniques have been developed for the production of antibody fragments. Traditionally, these fragments were derived via proteolytic digestion of intact antibodies (see, e.g., Morimoto et al., *Journal of Biochemical and Biophysical Methods* 24:107-117 (1992); and Brennan et al., *Science*, 229:81 (1985)). However, these fragments can now be produced directly by recombinant host cells. Fab, Fv and ScFv antibody fragments can all be expressed in and secreted from *E. coli*, thus allowing the facile production of large amounts of these fragments. Antibody fragments can be isolated from the antibody phage libraries discussed above. Alternatively, Fab'-SH fragments can be directly recovered from *E. coli* and chemically coupled to form F(ab')₂ fragments (Carter et al., *Bio/Technology* 10:163-167 (1992)). According to another approach, F(ab')₂ fragments can be isolated directly from recombinant host cell culture. Fab and F(ab')₂ fragment with increased in vivo half-life comprising a salvage receptor binding epitope residues are described in U.S. Pat. No. 5,869,046. Other techniques for the production of antibody fragments will be apparent to the skilled practitioner. In other embodiments, the antibody of choice is a single chain Fv fragment (scFv). See WO 93/16185; U.S. Pat. No. 5,571,894; and U.S. Pat. No. 5,587,458. Fv and sFv are the only species with intact combining sites that are devoid of constant regions; thus, they are suitable for reduced nonspecific bind-

ing during in vivo use. sFv fusion proteins may be constructed to yield fusion of an effector protein at either the amino or the carboxy terminus of an sFv. See *Antibody Engineering*, ed. Borrebaeck, supra. The antibody fragment may also be a "linear antibody", e.g., as described in U.S. Pat. No. 5,641,870 for example. Such linear antibody fragments may be monospecific or bispecific.

5. Bispecific Antibodies

Bispecific antibodies are antibodies that have binding specificities for at least two different epitopes. Exemplary bispecific antibodies may bind to two different epitopes of a TAHO protein as described herein. Other such antibodies may combine a TAHO binding site with a binding site for another protein. Alternatively, an anti-TAHO arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD3), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16), so as to focus and localize cellular defense mechanisms to the TAHO-expressing cell. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express TAHO. These antibodies possess a TAHO-binding arm and an arm which binds the cytotoxic agent (e.g., saporin, anti-interferon-α, vinca alkaloid, ricin A chain, methotrexate or radioactive isotope hapten). Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g., F(ab')₂ bispecific antibodies).

WO 96/16673 describes a bispecific anti-ErbB2/anti-FcγRIII antibody and U.S. Pat. No. 5,837,234 discloses a bispecific anti-ErbB2/anti-FcγRI antibody. A bispecific anti-ErbB2/Fc antibody is shown in WO98/02463. U.S. Pat. No. 5,821,337 teaches a bispecific anti-ErbB2/anti-CD3 antibody.

Methods for making bispecific antibodies are known in the art. Traditional production of full length bispecific antibodies is based on the co-expression of two immunoglobulin heavy chain-light chain pairs, where the two chains have different specificities (Millstein et al., *Nature* 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of 10 different antibody molecules, of which only one has the correct bispecific structure. Purification of the correct molecule, which is usually done by affinity chromatography steps, is rather cumbersome, and the product yields are low. Similar procedures are disclosed in WO 93/08829, and in Traunecker et al., *EMBO J.* 10:3655-3659 (1991).

According to a different approach, antibody variable domains with the desired binding specificities (antibody-antigen combining sites) are fused to immunoglobulin constant domain sequences. Preferably, the fusion is with an Ig heavy chain constant domain, comprising at least part of the hinge, C_{H2}, and C_{H3} regions. It is preferred to have the first heavy-chain constant region (C_{H1}) containing the site necessary for light chain bonding, present in at least one of the fusions. DNAs encoding the immunoglobulin heavy chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host cell. This provides for greater flexibility in adjusting the mutual proportions of the three polypeptide fragments in embodiments when unequal ratios of the three polypeptide chains used in the construction provide the optimum yield of the desired bispecific antibody. It is, however, possible to insert the coding sequences for two or all three polypeptide chains into a single expression vector when the expression of at least two polypeptide chains in equal ratios results in high yields or when the ratios have no significant affect on the yield of the desired chain combination.

In a preferred embodiment of this approach, the bispecific antibodies are composed of a hybrid immunoglobulin heavy chain with a first binding specificity in one arm, and a hybrid immunoglobulin heavy chain-light chain pair (providing a second binding specificity) in the other arm. It was found that this asymmetric structure facilitates the separation of the desired bispecific compound from unwanted immunoglobulin chain combinations, as the presence of an immunoglobulin light chain in only one half of the bispecific molecule provides for a facile way of separation. This approach is disclosed in WO 94/04690. For further details of generating bispecific antibodies see, for example, Suresh et al., *Methods in Enzymology* 121:210 (1986).

According to another approach described in U.S. Pat. No. 5,731,168, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the C_{H3} domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g., tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g., alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies include cross-linked or "heteroconjugate" antibodies. For example, one of the antibodies in the heteroconjugate can be coupled to avidin, the other to biotin. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Pat. No. 4,676,980), and for treatment of 1.5 HIV infection (WO 91/00360, WO 92/200373, and EP 03089). Heteroconjugate antibodies may be made using any convenient cross-linking methods. Suitable cross-linking agents are well known in the art, and are disclosed in U.S. Pat. No. 4,676,980, along with a number of cross-linking techniques.

Techniques for generating bispecific antibodies from antibody fragments have also been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., *Science* 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent, sodium arsenite, to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Recent progress has facilitated the direct recovery of Fab'-SH fragments from *E. coli*, which can be chemically coupled to form bispecific antibodies. Shalaby et al., *J. Exp. Med.* 175: 217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets. Various techniques for making and isolating bispecific antibody frag-

ments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., *J. Immunol.* 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., *Proc. Natl. Acad. Sci. USA* 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a V_H connected to a V_L by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (scFv) dimers has also been reported. See Gruber et al., *J. Immunol.*, 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., *J. Immunol.* 147:60 (1991).

6. Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Pat. No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Pat. No. 4,676,980.

7. Multivalent Antibodies

A multivalent antibody may be internalized (and/or catabolized) faster than a bivalent antibody by a cell expressing an antigen to which the antibodies bind. The antibodies of the present invention can be multivalent antibodies (which are other than of the IgM class) with three or more antigen binding sites (e.g. tetravalent antibodies), which can be readily produced by recombinant expression of nucleic acid encoding the polypeptide chains of the antibody. The multivalent antibody can comprise a dimerization domain and three or more antigen binding sites. The preferred dimerization domain comprises (or consists of) an Fc region or a hinge region. In this scenario, the antibody will comprise an Fc region and three or more antigen binding sites amino-terminal to the Fc region. The preferred multivalent antibody herein comprises (or consists of) three to about eight, but preferably four, antigen binding sites. The multivalent antibody comprises at least one polypeptide chain (and preferably two polypeptide chains), wherein the polypeptide chain(s) comprise two or more variable domains. For instance, the polypeptide chain(s) may comprise VD1-(X1)_n-VD2-(X2)_m-Fc, wherein VD1 is a first variable domain, VD2 is a second variable domain, Fc is one polypeptide chain of an Fc region, X1 and X2 represent an amino acid or polypeptide, and n is 0 or 1. For instance, the polypeptide chain(s) may comprise: VH-CH1-flexible linker-VH-CH1-Fc region chain; or VH-CH1-VH-CH1-Fc region chain. The multivalent antibody herein preferably further comprises at

least two (and preferably four) light chain variable domain polypeptides. The multivalent antibody herein may, for instance, comprise from about two to about eight light chain variable domain polypeptides. The light chain variable domain polypeptides contemplated here comprise a light chain variable domain and, optionally, further comprise a CL domain.

8. Effector Function Engineering

It may be desirable to modify the antibody of the invention with respect to effector function, e.g., so as to enhance antigen-dependent cell-mediated cytotoxicity (ADCC) and/or complement dependent cytotoxicity (CDC) of the antibody. This may be achieved by introducing one or more amino acid substitutions in an Fc region of the antibody. Alternatively or additionally, cysteine residue(s) may be introduced in the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., *J. Exp. Med.* 176:1191-1195 (1992) and Shopes, B. *J. Immunol.* 148:2918-2922 (1992). Homodimeric antibodies with enhanced antitumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff et al. *Cancer Research* 53:2560-2565 (1993). Alternatively, an antibody can be engineered which has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al. *Anti-Cancer Drug Design* 3:219-230 (1989). To increase the serum half life of the antibody, one may incorporate a salvage receptor binding epitope into the antibody (especially an antibody fragment) as described in U.S. Pat. No. 5,739,277, for example. As used herein, the term "salvage receptor binding epitope" refers to an epitope of the Fc region of an IgG molecule (e.g., IgG₁, IgG₂, IgG₃, or IgG₄) that is responsible for increasing the in vivo serum half-life of the IgG molecule.

9. Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, a growth inhibitory agent, a toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolaca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radioisotopes are available for the production of radioconjugated antibodies. Examples include ²¹²Bi, ¹³¹I, ¹³¹In, ⁹⁰Y, and ¹⁸⁶Re. Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyl)dithiol propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in

Vitetta et al., *Science*, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminopentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

Conjugates of an antibody and one or more small molecule toxins, such as a calicheamicin, auristatin peptides, such as monomethylauristatin (MMAE) (synthetic analog of dolastatin), maytansinoids, such as DM1, a trichothene, and CC1065, and the derivatives of these toxins that have toxin activity, are also contemplated herein.

Maytansine and Maytansinoids

In one preferred embodiment, an anti-TAHO antibody (full length or fragments) of the invention is conjugated to one or more maytansinoid molecules.

Maytansinoids, such as DM1, are mitototic inhibitors which act by inhibiting tubulin polymerization. Maytansine was first isolated from the east African shrub *Maytenus serrata* (U.S. Pat. No. 3,896,111). Subsequently, it was discovered that certain microbes also produce maytansinoids, such as maytansinol and C-3 maytansinol esters (U.S. Pat. No. 4,151,042). Synthetic maytansinol and derivatives and analogues thereof are disclosed, for example, in U.S. Pat. Nos. 4,137,230; 4,248,870; 4,256,746; 4,260,608; 4,265,814; 4,294,757; 4,307,016; 4,308,268; 4,308,269; 4,309,428; 4,313,946; 4,315,929; 4,317,821; 4,322,348; 4,331,598; 4,361,650; 4,364,866; 4,424,219; 4,450,254; 4,362,663; and 4,371,533, the disclosures of which are hereby expressly incorporated by reference.

Maytansinoid-Antibody Conjugates

In an attempt to improve their therapeutic index, maytansine and maytansinoids have been conjugated to antibodies specifically binding to tumor cell antigens. Immunoconjugates containing maytansinoids and their therapeutic use are disclosed, for example, in U.S. Pat. Nos. 5,208,020, 5,416,064 and European Patent EP 0 425 235 B1, the disclosures of which are hereby expressly incorporated by reference. Liu et al., *Proc. Natl. Acad. Sci. USA* 93:8618-8623 (1996) described immunoconjugates comprising a maytansinoid designated DM1 linked to the monoclonal antibody C242 directed against human colorectal cancer. The conjugate was found to be highly cytotoxic towards cultured colon cancer cells, and showed antitumor activity in an in vivo tumor growth assay. Chari et al., *Cancer Research* 52:127-131 (1992) describe immunoconjugates in which a maytansinoid was conjugated via a disulfide linker to the murine antibody A7 binding to an antigen on human colon cancer cell lines, or to another murine monoclonal antibody TA.1 that binds the HER-2/neu oncogene. The cytotoxicity of the TA.1-maytansinoid conjugate was tested in vitro on the human breast cancer cell line SK-BR-3, which expresses 3×10^5 HER-2 surface antigens per cell. The drug conjugate achieved a degree of cytotoxicity similar to the free maytansinoid drug, which could be increased by increasing the number of maytansinoid molecules per antibody molecule. The A7-maytansinoid conjugate showed low systemic cytotoxicity in mice.

Anti-TAHO Polypeptide Antibody-Maytansinoid Conjugates (Immunoconjugates)

Anti-TAHO antibody-maytansinoid conjugates are prepared by chemically linking an anti-TAHO antibody to a maytansinoid molecule without significantly diminishing the biological activity of either the antibody or the maytansinoid molecule. An average of 3-4 maytansinoid molecules conjugated per antibody molecule has shown efficacy in enhancing cytotoxicity of target cells without negatively affecting the function or solubility of the antibody, although even one

molecule of toxin/antibody would be expected to enhance cytotoxicity over the use of naked antibody. Maytansinoids are well known in the art and can be synthesized by known techniques or isolated from natural sources. Suitable maytansinoids are disclosed, for example, in U.S. Pat. No. 5,208,020 and in the other patents and nonpatent publications referred to hereinabove. Preferred maytansinoids are maytansinol and maytansinol analogues modified in the aromatic ring or at other positions of the maytansinol molecule, such as various maytansinol esters.

There are many linking groups known in the art for making antibody-maytansinoid conjugates, including, for example, those disclosed in U.S. Pat. No. 5,208,020 or EP Patent 0 425 235 B1, and Chari et al., *Cancer Research* 52:127-131 (1992). The linking groups include disulfide groups, thioether groups, acid labile groups, photolabile groups, peptidase labile groups, or esterase labile groups, as disclosed in the above-identified patents, disulfide and thioether groups being preferred.

Conjugates of the antibody and maytansinoid may be made using a variety of bifunctional protein coupling agents such as N-succinimidyl-3-(2-pyridylthio) propionate (SPDP), succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate, iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as toluene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). Particularly preferred coupling agents include N-succinimidyl-3-(2-pyridylthio) propionate (SPDP) (Carlsson et al., *Biochem. J.* 173:723-737 [1978]), sulfosuccinimidyl maleimidomethyl cyclohexane carboxylate (SMCC) and N-succinimidyl-4-(2-pyridylthio)pentanoate (SPP) to provide for a disulfide linkage. Other useful linkers include cysteine-MC-vc-PAB (a valine-citrulline (vc) dipeptide linker reagent having a maleimide component and a para-aminobenzyl carbamoyl (PAB) self-immolative component).

The linker may be attached to the maytansinoid molecule at various positions, depending on the type of the link. For example, an ester linkage may be formed by reaction with a hydroxyl group using conventional coupling techniques. The reaction may occur at the C-3 position having a hydroxyl group, the C-14 position modified with hydroxymethyl, the C-15 position modified with a hydroxyl group, and the C-20 position having a hydroxyl group. In a preferred embodiment, the linkage is formed at the C-3 position of maytansinol or a maytansinol analogue.

Calicheamicin

Another immunoconjugate of interest comprises an anti-TAHO antibody conjugated to one or more calicheamicin molecules. The calicheamicin family of antibiotics are capable of producing double-stranded DNA breaks at subpicomolar concentrations. For the preparation of conjugates of the calicheamicin family, see U.S. Pat. Nos. 5,712,374, 5,714,586, 5,739,116, 5,767,285, 5,770,701, 5,770,710, 5,773,001, 5,877,296 (all to American Cyanamid Company). Structural analogues of calicheamicin which may be used include, but are not limited to, γ_1^I , α_2^I , α_3^I , N-acetyl- γ_1^I , PSAG and θ_1^I (Hinman et al., *Cancer Research* 53:3336-3342 (1993), Lode et al., *Cancer Research* 58:2925-2928 (1998) and the aforementioned U.S. patents to American Cyanamid). Another anti-tumor drug that the antibody can be conjugated is QFA which is an antifolate. Both calicheamicin and QFA have intracellular sites of action and do not readily

cross the plasma membrane. Therefore, cellular uptake of these agents through antibody mediated internalization greatly enhances their cytotoxic effects.

Other Cytotoxic Agents

Other antitumor agents that can be conjugated to the anti-TAHO antibodies of the invention include BCNU, streptozocin, vincristine and 5-fluorouracil, the family of agents known collectively LL-E33288 complex described in U.S. Pat. Nos. 5,053,394, 5,770,710, as well as esperamicins (U.S. Pat. No. 5,877,296).

Enzymatically active toxins and fragments thereof which can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolaca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin and the tricothecenes. See, for example, WO 93/21232 published Oct. 28, 1993.

The present invention further contemplates an immunconjugate formed between an antibody and a compound with nucleolytic activity (e.g., a ribonuclease or a DNA endonuclease such as a deoxyribonuclease; DNase).

For selective destruction of the tumor, the antibody may comprise a highly radioactive atom. A variety of radioactive isotopes are available for the production of radioconjugated anti-TAHO antibodies. Examples include At^{211} , I^{131} , I^{125} , Y^{90} , Re^{186} , Re^{188} , Sm^{153} , Bi^{212} , P^{32} , Pb^{212} and radioactive isotopes of Lu. When the conjugate is used for detection, it may comprise a radioactive atom for scintigraphic studies, for example tc^{99m} or I^{123} , or a spin label for nuclear magnetic resonance (NMR) imaging (also known as magnetic resonance imaging, mri), such as iodine-123 again, iodine-131, indium-111, fluorine-19, carbon-13, nitrogen-15, oxygen-17, gadolinium, manganese or iron.

The radio- or other labels may be incorporated in the conjugate in known ways. For example, the peptide may be biosynthesized or may be synthesized by chemical amino acid synthesis using suitable amino acid precursors involving, for example, fluorine-19 in place of hydrogen. Labels such as tc^{99m} or I^{123} , Re^{186} , Re^{188} and In^{111} can be attached via a cysteine residue in the peptide. Yttrium-90 can be attached via a lysine residue. The IODOGEN method (Fraker et al (1978) Biochem. Biophys. Res. Commun. 80: 49-57 can be used to incorporate iodine-123. "Monoclonal Antibodies in Immunoscintigraphy" (Chatal, CRC Press 1989) describes other methods in detail.

Conjugates of the antibody and cytotoxic agent may be made using a variety of bifunctional protein coupling agents such as N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP), succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate, iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., *Science* 238:1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyl-diethylene triamine-pentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026. The linker may be a "cleavable linker" facilitating release of the cytotoxic drug in the cell. For example, an

acid-labile linker, peptidase-sensitive linker, photolabile linker, dimethyl linker or disulfide-containing linker (Chari et al., *Cancer Research* 52:127-131 (1992); U.S. Pat. No. 5,208,020) may be used.

Alternatively, a fusion protein comprising the anti-TAHO antibody and cytotoxic agent may be made, e.g., by recombinant techniques or peptide synthesis. The length of DNA may comprise respective regions encoding the two portions of the conjugate either adjacent one another or separated by a region encoding a linker peptide which does not destroy the desired properties of the conjugate.

In yet another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pre-targeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) which is conjugated to a cytotoxic agent (e.g., a radionucleotide).

10. Immunoliposomes

The anti-TAHO antibodies disclosed herein may also be formulated as immunoliposomes. A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein et al., *Proc. Natl. Acad. Sci. USA* 82:3688 (1985); Hwang et al., *Proc. Natl. Acad. Sci. USA* 77:4030 (1980); U.S. Pat. Nos. 4,485,045 and 4,544,545; and WO97/38731 published Oct. 23, 1997. Liposomes with enhanced circulation time are disclosed in U.S. Pat. No. 5,013,556.

Particularly useful liposomes can be generated by the reverse phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin et al., *J. Biol. Chem.* 257: 286-288 (1982) via a disulfide interchange reaction. A chemotherapeutic agent is optionally contained within the liposome. See Gabizon et al., *J. National Cancer Inst.* 81(19): 1484 (1989).

B. TAHO Binding Oligopeptides

TAHO binding oligopeptides of the present invention are oligopeptides that bind, preferably specifically, to a TAHO polypeptide as described herein. TAHO binding oligopeptides may be chemically synthesized using known oligopeptide synthesis methodology or may be prepared and purified using recombinant technology. TAHO binding oligopeptides are usually at least about 5 amino acids in length, alternatively at least about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 amino acids in length or more, wherein such oligopeptides that are capable of binding, preferably specifically, to a TAHO polypeptide as described herein. TAHO binding oligopeptides may be identified without undue experimentation using well known techniques. In this regard, it is noted that techniques for screening oligopeptide libraries for oligopeptides that are capable of specifically binding to a polypeptide target

are well known in the art (see, e.g., U.S. Pat. Nos. 5,556,762, 5,750,373, 4,708,871, 4,833,092, 5,223,409, 5,403,484, 5,571,689, 5,663,143; PCT Publication Nos. WO 84/03506 and WO84/03564; Geysen et al., *Proc. Natl. Acad. Sci. U.S.A.*, 81:3998-4002 (1984); Geysen et al., *Proc. Natl. Acad. Sci. U.S.A.*, 82:178-182 (1985); Geysen et al., in *Synthetic Peptides as Antigens*, 130-149 (1986); Geysen et al., *J. Immunol. Meth.*, 102:259-274 (1987); Schoofs et al., *J. Immunol.*, 140:611-616 (1988), Cwirla, S. E. et al. (1990) *Proc. Natl. Acad. Sci. USA*, 87:6378; Lowman, H. B. et al. (1991) *Biochemistry*, 30:10832; Clackson, T. et al. (1991) *Nature*, 352: 624; Marks, J. D. et al. (1991), *J. Mol. Biol.*, 222:581; Kang, A. S. et al. (1991) *Proc. Natl. Acad. Sci. USA*, 88:8363, and Smith, G. P. (1991) *Current Opin. Biotechnol.*, 2:668).

In this regard, bacteriophage (phage) display is one well known technique which allows one to screen large oligopeptide libraries to identify member(s) of those libraries which are capable of specifically binding to a polypeptide target. Phage display is a technique by which variant polypeptides are displayed as fusion proteins to the coat protein on the surface of bacteriophage particles (Scott, J. K. and Smith, G. P. (1990) *Science* 249: 386). The utility of phage display lies in the fact that large libraries of selectively randomized protein variants (or randomly cloned cDNAs) can be rapidly and efficiently sorted for those sequences that bind to a target molecule with high affinity. Display of peptide (Cwirla, S. E. et al. (1990) *Proc. Natl. Acad. Sci. USA*, 87:6378) or protein (Lowman, H. B. et al. (1991) *Biochemistry*, 30:10832; Clackson, T. et al. (1991) *Nature*, 352: 624; Marks, J. D. et al. (1991), *J. Mol. Biol.*, 222:581; Kang, A. S. et al. (1991) *Proc. Natl. Acad. Sci. USA*, 88:8363) libraries on phage have been used for screening millions of polypeptides or oligopeptides for ones with specific binding properties (Smith, G. P. (1991) *Current Opin. Biotechnol.*, 2:668). Sorting phage libraries of random mutants requires a strategy for constructing and propagating a large number of variants, a procedure for affinity purification using the target receptor, and a means of evaluating the results of binding enrichments. U.S. Pat. Nos. 5,223,409, 5,403,484, 5,571,689, and 5,663,143.

Although most phage display methods have used filamentous phage, lambdoid phage display systems (WO 95/34683; U.S. Pat. No. 5,627,024), T4 phage display systems (Ren et al., *Gene*, 215: 439 (1998); Zhu et al., *Cancer Research*, 58(15): 3209-3214 (1998); Jiang et al., *Infection & Immunity*, 65(11): 4770-4777 (1997); Ren et al., *Gene*, 195(2):303-311 (1997); Ren, *Protein Sci.*, 5: 1833 (1996); Efimov et al., *Virus Genes*, 10: 173 (1995)) and T7 phage display systems (Smith and Scott, *Methods in Enzymology*, 217: 228-257 (1993); U.S. Pat. No. 5,766,905) are also known.

Many other improvements and variations of the basic phage display concept have now been developed. These improvements enhance the ability of display systems to screen peptide libraries for binding to selected target molecules and to display functional proteins with the potential of screening these proteins for desired properties. Combinatorial reaction devices for phage display reactions have been developed (WO 98/14277) and phage display libraries have been used to analyze and control bimolecular interactions (WO 98/20169; WO 98/20159) and properties of constrained helical peptides (WO 98/20036). WO 97/35196 describes a method of isolating an affinity ligand in which a phage display library is contacted with one solution in which the ligand will bind to a target molecule and a second solution in which the affinity ligand will not bind to the target molecule, to selectively isolate binding ligands. WO 97/46251 describes a method of biopanning a random phage display library with an affinity purified antibody and then isolating binding phage,

followed by a micropanning process using microplate wells to isolate high affinity binding phage. The use of *Staphylococcus aureus* protein A as an affinity tag has also been reported (Li et al. (1998) *MolBiotech.*, 9:187). WO 97/47314 describes the use of substrate subtraction libraries to distinguish enzyme specificities using a combinatorial library which may be a phage display library. A method for selecting enzymes suitable for use in detergents using phage display is described in WO 97/09446. Additional methods of selecting specific binding proteins are described in U.S. Pat. Nos. 5,498,538, 5,432,018, and WO 98/15833.

Methods of generating peptide libraries and screening these libraries are also disclosed in U.S. Pat. Nos. 5,723,286, 5,432,018, 5,580,717, 5,427,908, 5,498,530, 5,770,434, 5,734,018, 5,698,426, 5,763,192, and 5,723,323.

C. TAHO Binding Organic Molecules

TAHO binding organic molecules are organic molecules other than oligopeptides or antibodies as defined herein that bind, preferably specifically, to a TAHO polypeptide as described herein. TAHO binding organic molecules may be identified and chemically synthesized using known methodology (see, e.g., PCT Publication Nos. WO00/00823 and WO00/39585). TAHO binding organic molecules are usually less than about 2000 daltons in size, alternatively less than about 1500, 750, 500, 250 or 200 daltons in size, wherein such organic molecules that are capable of binding, preferably specifically, to a TAHO polypeptide as described herein may be identified without undue experimentation using well known techniques. In this regard, it is noted that techniques for screening organic molecule libraries for molecules that are capable of binding to a polypeptide target are well known in the art (see, e.g., PCT Publication Nos. WO00/00823 and WO00/39585). TAHO binding organic molecules may be, for example, aldehydes, ketones, oximes, hydrazones, semicarbazones, carbazides, primary amines, secondary amines, tertiary amines, N-substituted hydrazines, hydrazides, alcohols, ethers, thiols, thioethers, disulfides, carboxylic acids, esters, amides, ureas, carbamates, carbonates, ketals, thioketals, acetals, thioacetals, aryl halides, aryl sulfonates, alkyl halides, alkyl sulfonates, aromatic compounds, heterocyclic compounds, anilines, alkenes, alkynes, diols, amino alcohols, oxazolidines, oxazolines, thiazolidines, thiazolines, enamines, sulfonamides, epoxides, aziridines, isocyanates, sulfonyl chlorides, diazo compounds, acid chlorides, or the like.

D. Screening for Anti-TAHO Antibodies, TAHO Binding Oligopeptides and TAHO Binding Organic Molecules with the Desired Properties

Techniques for generating antibodies, oligopeptides and organic molecules that bind to TAHO polypeptides have been described above. One may further select antibodies, oligopeptides or other organic molecules with certain biological characteristics, as desired.

The growth inhibitory effects of an anti-TAHO antibody, oligopeptide or other organic molecule of the invention may be assessed by methods known in the art, e.g., using cells which express a TAHO polypeptide either endogenously or following transfection with the TAHO gene. For example, appropriate tumor cell lines and TAHO-transfected cells may be treated with an anti-TAHO monoclonal antibody, oligopeptide or other organic molecule of the invention at various concentrations for a few days (e.g., 2-7) days and stained with crystal violet or MTT or analyzed by some other colorimetric assay. Another method of measuring proliferation would be by comparing ³H-thymidine uptake by the cells treated in the presence or absence an anti-TAHO antibody, TAHO binding oligopeptide or TAHO binding organic molecule of the invention. After treatment, the cells are harvested

and the amount of radioactivity incorporated into the DNA quantitated in a scintillation counter. Appropriate positive controls include treatment of a selected cell line with a growth inhibitory antibody known to inhibit growth of that cell line. Growth inhibition of tumor cells *in vivo* can be determined in various ways known in the art. The tumor cell may be one that overexpresses a TAHO polypeptide. The anti-TAHO antibody, TAHO binding oligopeptide or TAHO binding organic molecule will inhibit cell proliferation of a TAHO-expressing tumor cell *in vitro* or *in vivo* by about 25-100% compared to the untreated tumor cell, more preferably, by about 30-100%, and even more preferably by about 50-100% or 70-100%, in one embodiment, at an antibody concentration of about 0.5 to 30 µg/ml. Growth inhibition can be measured at an antibody concentration of about 0.5 to 3 µg/ml or about 0.5 nM to 200 nM in cell culture, where the growth inhibition is determined 1-10 days after exposure of the tumor cells to the antibody. The antibody is growth inhibitory *in vivo* if administration of the anti-TAHO antibody at about 1 µg/kg to about 100 mg/kg body weight results in reduction in tumor size or reduction of tumor cell proliferation within about 5 days to 3 months from the first administration of the antibody, preferably within about 5 to 30 days.

To select for an anti-TAHO antibody, TAHO binding oligopeptide or TAHO binding organic molecule which induces cell death, loss of membrane integrity as indicated by, e.g., propidium iodide (PI), trypan blue or 7AAD uptake may be assessed relative to control. A PI uptake assay can be performed in the absence of complement and immune effector cells. TAHO polypeptide-expressing tumor cells are incubated with medium alone or medium containing the appropriate anti-TAHO antibody (e.g., at about 10 µg/ml), TAHO binding oligopeptide or TAHO binding organic molecule. The cells are incubated for a 3 day time period. Following each treatment, cells are washed and aliquoted into 35 mm strainer-capped 12x75 tubes (1 ml per tube, 3 tubes per treatment group) for removal of cell clumps. Tubes then receive PI (10 µg/ml). Samples may be analyzed using a FACSCAN® flow cytometer and FACSCONVERT® CellQuest software (Becton Dickinson). Those anti-TAHO antibodies, TAHO binding oligopeptides or TAHO binding organic molecules that induce statistically significant levels of cell death as determined by PI uptake may be selected as cell death-inducing anti-TAHO antibodies, TAHO binding oligopeptides or TAHO binding organic molecules.

To screen for antibodies, oligopeptides or other organic molecules which bind to an epitope on a TAHO polypeptide bound by an antibody of interest, a routine cross-blocking assay such as that described in *Antibodies, A Laboratory Manual*, Cold Spring Harbor Laboratory, Ed Harlow and David Lane (1988), can be performed. This assay can be used to determine if a test antibody, oligopeptide or other organic molecule binds the same site or epitope as a known anti-TAHO antibody. Alternatively, or additionally, epitope mapping can be performed by methods known in the art. For example, the antibody sequence can be mutagenized such as by alanine scanning, to identify contact residues. The mutant antibody is initially tested for binding with polyclonal antibody to ensure proper folding. In a different method, peptides corresponding to different regions of a TAHO polypeptide can be used in competition assays with the test antibodies or with a test antibody and an antibody with a characterized or known epitope.

E. Antibody Dependent Enzyme Mediated Prodrug Therapy (ADEPT)

The antibodies of the present invention may also be used in ADEPT by conjugating the antibody to a prodrug-activating

enzyme which converts a prodrug (e.g., a peptidyl chemotherapeutic agent, see WO81/01145) to an active anti-cancer drug. See, for example, WO 88/07378 and U.S. Pat. No. 4,975,278.

The enzyme component of the immunoconjugate useful for ADEPT includes any enzyme capable of acting on a prodrug in such a way so as to convert it into its more active, cytotoxic form.

Enzymes that are useful in the method of this invention include, but are not limited to, alkaline phosphatase useful for converting phosphate-containing prodrugs into free drugs; arylsulfatase useful for converting sulfate-containing prodrugs into free drugs; cytosine deaminase useful for converting non-toxic 5-fluorocytosine into the anti-cancer drug, 5-fluorouracil; proteases, such as serratia protease, thermolysin, subtilisin, carboxypeptidases and cathepsins (such as cathepsins B and L), that are useful for converting peptide-containing prodrugs into free drugs; D-alanylcarboxypeptidases, useful for converting prodrugs that contain D-amino acid substituents; carbohydrate-cleaving enzymes such as β-galactosidase and neuraminidase useful for converting glycosylated prodrugs into free drugs; β-lactamase useful for converting drugs derivatized with β-lactams into free drugs; and penicillin amidases, such as penicillin V amidase or penicillin G amidase, useful for converting drugs derivatized at their amine nitrogens with phenoxyacetyl or phenylacetyl groups, respectively, into free drugs. Alternatively, antibodies with enzymatic activity, also known in the art as "abzymes", can be used to convert the prodrugs of the invention into free active drugs (see, e.g., Massey, *Nature* 328:457-458 (1987)). Antibody-abzyme conjugates can be prepared as described herein for delivery of the abzyme to a tumor cell population.

The enzymes of this invention can be covalently bound to the anti-TAHO antibodies by techniques well known in the art such as the use of the heterobifunctional crosslinking reagents discussed above. Alternatively, fusion proteins comprising at least the antigen binding region of an antibody of the invention linked to at least a functionally active portion of an enzyme of the invention can be constructed using recombinant DNA techniques well known in the art (see, e.g., Neuberger et al., *Nature* 312:604-608 (1984)).

F. Full-Length TAHO Polypeptides

The present invention also provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as TAHO polypeptides. In particular, cDNAs (partial and full-length) encoding various TAHO polypeptides have been identified and isolated, as disclosed in further detail in the Examples below.

As disclosed in the Examples below, various cDNA clones have been deposited with the ATCC. The actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the TAHO polypeptides and encoding nucleic acids described herein, in some cases, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

G. Anti-TAHO Antibody and TAHO Polypeptide Variants

In addition to the anti-TAHO antibodies and full-length native sequence TAHO polypeptides described herein, it is contemplated that anti-TAHO antibody and TAHO polypeptide variants can be prepared. Anti-TAHO antibody and TAHO polypeptide variants can be prepared by introducing appropriate nucleotide changes into the encoding DNA, and/or by synthesis of the desired antibody or polypeptide. Those skilled in the art will appreciate that amino acid changes may

alter post-translational processes of the anti-TAHO antibody or TAHO polypeptide, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

Variations in the anti-TAHO antibodies and TAHO polypeptides described herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Pat. No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the antibody or polypeptide that results in a change in the amino acid sequence as compared with the native sequence antibody or polypeptide. Optionally the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the anti-TAHO antibody or TAHO polypeptide. Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the anti-TAHO antibody or TAHO polypeptide with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

Anti-TAHO antibody and TAHO polypeptide fragments are provided herein. Such fragments may be truncated at the N-terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native antibody or protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the anti-TAHO antibody or TAHO polypeptide.

Anti-TAHO antibody and TAHO polypeptide fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating antibody or polypeptide fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired antibody or polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, anti-TAHO antibody and TAHO polypeptide fragments share at least one biological and/or immunological activity with the native anti-TAHO antibody or TAHO polypeptide disclosed herein.

In particular embodiments, conservative substitutions of interest are shown in Table 6 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 6, or as further described below in reference to amino acid classes, are introduced and the products screened.

TABLE 6

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	val; leu; ile	val
Arg (R)	lys; gln; asn	lys
Asn (N)	gln; his; lys; arg	gln
Asp (D)	glu	glu
Cys (C)	ser	ser
Gln (Q)	asn	asn
Glu (E)	asp	asp
Gly (G)	pro; ala	ala
His (H)	asn; gln; lys; arg	arg
Ile (I)	leu; val; met; ala; phe; norleucine	leu
Leu (L)	norleucine; ile; val; met; ala; phe	ile
Lys (K)	arg; gln; asn	arg
Met (M)	leu; phe; ile	leu
Phe (F)	leu; val; ile; ala; tyr	leu
Pro (P)	ala	ala
Ser (S)	thr	thr
Thr (T)	ser	ser
Trp (W)	tyr; phe	tyr
Tyr (Y)	trp; phe; thr; ser	phe
Val (V)	ile; leu; met; phe; ala; norleucine	leu

Substantial modifications in function or immunological identity of the anti-TAHO antibody or TAHO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

- (1) hydrophobic: norleucine, met, ala, val, leu, ile;
- (2) neutral hydrophilic: cys, ser, thr;
- (3) acidic: asp, glu;
- (4) basic: asn, gin, his, lys, arg;
- (5) residues that influence chain orientation: gly, pro; and
- (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., *Nucl. Acids Res.*, 13:4331 (1986); Zoller et al., *Nucl. Acids Res.*, 10:6487 (1987)], cassette mutagenesis [Wells et al., *Gene*, 34:315 (1985)], restriction selection mutagenesis [Wells et al., *Philos. Trans. R. Soc. London Ser.A*, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the anti-TAHO antibody or TAHO polypeptide variant DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, *Science*, 244:1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, *The Proteins*,

(W.H. Freeman & Co., N.Y.); Chothia, *J. Mol. Biol.*, 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

Any cysteine residue not involved in maintaining the proper conformation of the anti-TAHO antibody or TAHO polypeptide also may be substituted, generally with serine, to improve the oxidative stability of the molecule and prevent aberrant crosslinking. Conversely, cysteine bond(s) may be added to the anti-TAHO antibody or TAHO polypeptide to improve its stability (particularly where the antibody is an antibody fragment such as an Fv fragment).

A particularly preferred type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody (e.g., a humanized or human antibody). Generally, the resulting variant(s) selected for further development will have improved biological properties relative to the parent antibody from which they are generated. A convenient way for generating such substitutional variants involves affinity maturation using phage display. Briefly, several hypervariable region sites (e.g., 6-7 sites) are mutated to generate all possible amino substitutions at each site. The antibody variants thus generated are displayed in a monovalent fashion from filamentous phage particles as fusions to the gene III product of M13 packaged within each particle. The phage-displayed variants are then screened for their biological activity (e.g., binding affinity) as herein disclosed. In order to identify candidate hypervariable region sites for modification, alanine scanning mutagenesis can be performed to identify hypervariable region residues contributing significantly to antigen binding. Alternatively, or additionally, it may be beneficial to analyze a crystal structure of the antigen-antibody complex to identify contact points between the antibody and human TAHO polypeptide. Such contact residues and neighboring residues are candidates for substitution according to the techniques elaborated herein. Once such variants are generated, the panel of variants is subjected to screening as described herein and antibodies with superior properties in one or more relevant assays may be selected for further development.

Nucleic acid molecules encoding amino acid sequence variants of the anti-TAHO antibody are prepared by a variety of methods known in the art. These methods include, but are not limited to, isolation from a natural source (in the case of naturally occurring amino acid sequence variants) or preparation by oligonucleotide-mediated (or site-directed) mutagenesis, PCR mutagenesis, and cassette mutagenesis of an earlier prepared variant or a non-variant version of the anti-TAHO antibody.

H. Modifications of Anti-TAHO Antibodies and TAHO Polypeptides

Covalent modifications of anti-TAHO antibodies and TAHO polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of an anti-TAHO antibody or TAHO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C-terminal residues of the anti-TAHO antibody or TAHO polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking anti-TAHO antibody or TAHO polypeptide to a water-insoluble support matrix or surface for use in the method for purifying anti-TAHO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-

maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propionimide.

Other modifications include deamidation of glutamyl and asparagyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T. E. Creighton, *Proteins: Structure and Molecular Properties*, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the anti-TAHO antibody or TAHO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the antibody or polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence anti-TAHO antibody or TAHO polypeptide (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence anti-TAHO antibody or TAHO polypeptide. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

Glycosylation of antibodies and other polypeptides is typically either N-linked or O-linked. N-linked refers to the attachment of the carbohydrate moiety to the side chain of an asparagine residue. The tripeptide sequences asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline, are the recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. Thus, the presence of either of these tripeptide sequences in a polypeptide creates a potential glycosylation site. O-linked glycosylation refers to the attachment of one of the sugars N-acetylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used.

Addition of glycosylation sites to the anti-TAHO antibody or TAHO polypeptide is conveniently accomplished by altering the amino acid sequence such that it contains one or more of the above-described tripeptide sequences (for N-linked glycosylation sites). The alteration may also be made by the addition of, or substitution by, one or more serine or threonine residues to the sequence of the original anti-TAHO antibody or TAHO polypeptide (for O-linked glycosylation sites). The anti-TAHO antibody or TAHO polypeptide amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the anti-TAHO antibody or TAHO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the anti-TAHO antibody or TAHO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 Sep. 1987, and in Aplin and Wriston, *CRC Crit. Rev. Biochem.*, pp. 259-306 (1981).

Removal of carbohydrate moieties present on the anti-TAHO antibody or TAHO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., *Arch. Biochem. Biophys.*, 259:52 (1987) and by Edge et

al., *Anal. Biochem.*, 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., *Meth. Enzymol.*, 138:350 (1987).

Another type of covalent modification of anti-TAHO antibody or TAHO polypeptide comprises linking the antibody or polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Pat. No. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337. The antibody or polypeptide also may be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization (for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively), in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules), or in macroemulsions. Such techniques are disclosed in *Remington's Pharmaceutical Sciences*, 16th edition, Oslo, A., Ed., (1980).

The anti-TAHO antibody or TAHO polypeptide of the present invention may also be modified in a way to form chimeric molecules comprising an anti-TAHO antibody or TAHO polypeptide fused to another, heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the anti-TAHO antibody or TAHO polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl-terminus of the anti-TAHO antibody or TAHO polypeptide. The presence of such epitope-tagged forms of the anti-TAHO antibody or TAHO polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the anti-TAHO antibody or TAHO polypeptide to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., *Mol. Cell. Biol.*, 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., *Molecular and Cellular Biology*, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., *Protein Engineering*, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., *BioTechnology*, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., *Science*, 255:192-194 (1992)]; an α -tubulin epitope peptide [Skinner et al., *J. Biol. Chem.*, 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., *Proc. Natl. Acad. Sci. USA*, 87:6393-6397 (1990)].

In an alternative embodiment, the chimeric molecule may comprise a fusion of the anti-TAHO antibody or TAHO polypeptide with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of an anti-TAHO antibody or TAHO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH and CH₃, or the hinge, CH₁, CH₂ and CH₃ regions of an IgG1 molecule. For the production of immunoglobulin fusions see also U.S. Pat. No. 5,428,130 issued Jun. 27, 1995.

I. Preparation of Anti-TAHO Antibodies and TAHO Polypeptides

The description below relates primarily to production of anti-TAHO antibodies and TAHO polypeptides by culturing cells transformed or transfected with a vector containing anti-TAHO antibody- and TAHO polypeptide-encoding nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare anti-TAHO antibodies and TAHO polypeptides. For instance, the appropriate amino acid sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., *Solid-Phase Peptide Synthesis*, W.H. Freeman Co., San Francisco, Calif. (1969); Merrifield, *J. Am. Chem. Soc.*, 85:2149-2154 (1963)]. In vitro protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, Calif.) using manufacturer's instructions. Various portions of the anti-TAHO antibody or TAHO polypeptide may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the desired anti-TAHO antibody or TAHO polypeptide.

1. Isolation of DNA Encoding Anti-TAHO Antibody or TAHO Polypeptide

DNA encoding anti-TAHO antibody or TAHO polypeptide may be obtained from a cDNA library prepared from tissue believed to possess the anti-TAHO antibody or TAHO polypeptide mRNA and to express it at a detectable level. Accordingly, human anti-TAHO antibody or TAHO polypeptide DNA can be conveniently obtained from a cDNA library prepared from human tissue. The anti-TAHO antibody- or TAHO polypeptide-encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

Libraries can be screened with probes (such as oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual* (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding anti-TAHO antibody or TAHO polypeptide is to use PCR methodology [Sambrook et al., supra; Dieffenbach et al., *PCR Primer: A Laboratory Manual* (Cold Spring Harbor Laboratory Press, 1995)].

Techniques for screening a cDNA library are well known in the art. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like ³²P-labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., supra.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

2. Selection and Transformation of Host Cells

Host cells are transfected or transformed with expression or cloning vectors described herein for anti-TAHO antibody or TAHO polypeptide production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in *Mammalian Cell Biotechnology: a Practical Approach* M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example, CaCl₂, CaPO₄, liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., supra, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., *Gene*, 23:315 (1983) and WO 89/05859 published 29 Jun. 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, *Virology*, 52:456-457 (1978) can be employed. General aspects of mammalian cell host system transfections have been described in U.S. Pat. No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., *J. Bact.*, 130:946 (1977) and Hsiao et al., *Proc. Natl. Acad. Sci. (USA)*, 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., *Methods in Enzymology*, 185:527-537 (1990) and Mansour et al., *Nature*, 336:348-352 (1988).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as Bacilli such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 Apr. 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with

examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype tonA; *E. coli* W3110 strain 9E4, which has the complete genotype tonA ptr3; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype tonA ptr3 phoA E15 (argF-lac)169 degP ompT kah; *E. coli* W3110 strain 37D6, which has the complete genotype tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kah; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant degP deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Pat. No. 4,946,783 issued 7 Aug. 1990. Alternatively, in vitro methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

Full length antibody, antibody fragments, and antibody fusion proteins can be produced in bacteria, in particular when glycosylation and Fc effector function are not needed, such as when the therapeutic antibody is conjugated to a cytotoxic agent (e.g., a toxin) and the immunconjugate by itself shows effectiveness in tumor cell destruction. Full length antibodies have greater half life in circulation. Production in *E. coli* is faster and more cost efficient. For expression of antibody fragments and polypeptides in bacteria, see, e.g., U.S. Pat. No. 5,648,237 (Carter et. al.), U.S. Pat. No. 5,789,199 (Joly et al.), and U.S. Pat. No. 5,840,523 (Simmons et al.) which describes translation initiation regio (TIR) and signal sequences for optimizing expression and secretion, these patents incorporated herein by reference. After expression, the antibody is isolated from the *E. coli* cell paste in a soluble fraction and can be purified through, e.g., a protein A or G column depending on the isotype. Final purification can be carried out similar to the process for purifying antibody expressed e.g., in CHO cells.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for anti-TAHO antibody- or TAHO polypeptide-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, *Nature*, 290:140 [1981]; EP 139,383 published 2 May 1985); *Kluyveromyces* hosts (U.S. Pat. No. 4,943,529; Fleer et al., *Bio/Technology*, 9:968-975 (1991)) such as, e.g. lactis (MW98-8C, CBS683, CBS4574; Louvencourt et al., *J. Bacteriol.*, 154(2):737-742 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickeramii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilum* (ATCC 36,906; Van den Berg et al., *Bio/Technology*, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus*; *yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna et al., *J. Basic Microbiol.*, 28:265-278 [1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., *Proc. Natl. Acad. Sci. USA*, 76:5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 Oct. 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolyocladium* (WO 91/00357 published 10 Jan. 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., *Biochem. Biophys. Res. Commun.*, 112:284-289 [1983]; Tilburn et al., *Gene*, 26:205-221 [1983]; Yelton et al., *Proc. Natl. Acad. Sci. USA*, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, *EMBO J.*, 4:475-479 [1985]). Methylotropic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, *The Biochemistry of Methylotrophs*, 269 (1982).

Suitable host cells for the expression of glycosylated anti-TAHO antibody or TAHO polypeptide are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Spodoptera* Sf9, as well as plant cells, such as cell cultures of cotton, corn, potato, soybean, petunia, tomato, and tobacco. Numerous baculoviral strains and variants and corresponding permissive insect host cells from hosts such as *Spodoptera frugiperda* (caterpillar), *Aedes aegypti* (mosquito), *Aedes albopictus* (mosquito), *Drosophila melanogaster* (fruitfly), and *Bombyx mori* have been identified. A variety of viral strains for transfection are publicly available, e.g., the L-1 variant of *Autographa californica* NPV and the Bm-5 strain of *Bombyx mori* NPV, and such viruses may be used as the virus herein according to the present invention, particularly for transfection of *Spodoptera frugiperda* cells.

However, interest has been greatest in vertebrate cells, and propagation of vertebrate cells in culture (tissue culture) has become a routine procedure. Examples of useful mammalian host cell lines are monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., *J. Gen. Virol.* 36:59 (1977)); baby hamster kidney cells (BHK, ATCC CCL 10); Chinese hamster ovary cells/-DHFR (CHO, Urlaub et al., *Proc. Natl. Acad. Sci. USA* 77:4216 (1980)); mouse sertoli cells (TM4, Mather, *Biol. Reprod.* 23:243-251 (1980)); monkey kidney cells (CV1 ATCC CCL 70); African green monkey kidney cells (VERO-76, ATCC CRL-1587); human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); buffalo rat liver cells (BRL 3A, ATCC CRL 1442); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); mouse mammary tumor (MMT 060562, ATCC CCL51); TRI cells (Mather et al., *Annals N.Y. Acad. Sci.* 383:44-68 (1982)); MRC cells; FS4 cells; and a human hepatoma line (Hep G2).

Host cells are transformed with the above-described expression or cloning vectors for anti-TAHO antibody or TAHO polypeptide production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences.

3. Selection and Use of a Replicable Vector

The nucleic acid (e.g., cDNA or genomic DNA) encoding anti-TAHO antibody or TAHO polypeptide may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

The TAHO may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the anti-TAHO antibody- or TAHO polypeptide-encoding DNA that is inserted into the vector. The signal sequence may

be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, 1 pp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g., the yeast invertase leader, alpha factor leader (includes *Saccharomyces* and *Kluyveromyces* α -factor leaders, the latter described in U.S. Pat. No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 Apr. 1990), or the signal described in WO 90/13646 published 15 Nov. 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders.

Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 μ plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for Bacilli.

An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the anti-TAHO antibody- or TAHO polypeptide-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., *Proc. Natl. Acad. Sci. USA*, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., *Nature*, 282:39 (1979); Kingsman et al., *Gene*, 7:141 (1979); Tschemper et al., *Gene*, 10:157 (1980)]. The *trp1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-[Jones, *Genetics*, 85:12 (1977)].

Expression and cloning vectors usually contain a promoter operably linked to the anti-TAHO antibody- or TAHO polypeptide-encoding nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoters suitable for use with prokaryotic hosts include the β -lactamase and lactose promoter systems [Chang et al., *Nature*, 275:615 (1978); Goeddel et al., *Nature*, 281:544 (1979)], alkaline phosphatase, a tryptophan (*trp*) promoter system [Goeddel, *Nucleic Acids Res.*, 8:4057 (1980); EP 36,776], and hybrid promoters such as the *tac* promoter [deBoer et al., *Proc. Natl. Acad. Sci. USA*, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding anti-TAHO antibody or TAHO polypeptide.

Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., *J. Biol. Chem.*, 255:2073 (1980)] or other glycolytic enzymes [Hess et al., *J. Adv. Enzyme Reg.*, 7:149 (1968); Holland, *Biochemistry*, 17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase,

glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

Anti-TAHO antibody or TAHO polypeptide transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 Jul. 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

Transcription of a DNA encoding the anti-TAHO antibody or TAHO polypeptide by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin, α -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the anti-TAHO antibody or TAHO polypeptide coding sequence, but is preferably located at a site 5' from the promoter.

Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding anti-TAHO antibody or TAHO polypeptide.

Still other methods, vectors, and host cells suitable for adaptation to the synthesis of anti-TAHO antibody or TAHO polypeptide in recombinant vertebrate cell culture are described in Gething et al., *Nature*, 293:620-625 (1981); Mantei et al., *Nature*, 281:40-46 (1979); EP 117,060; and EP 117,058.

4. Culturing the Host Cells

The host cells used to produce the anti-TAHO antibody or TAHO polypeptide of this invention may be cultured in a variety of media. Commercially available media such as Ham's F10 (Sigma), Minimal Essential Medium (MEM), (Sigma), RPMI-1640 (Sigma), and Dulbecco's Modified Eagle's Medium (DMEM), Sigma are suitable for culturing the host cells. In addition, any of the media described in Ham et al., *Meth. Enz.* 58:44 (1979), Barnes et al., *Anal. Biochem.* 102:255 (1980), U.S. Pat. Nos. 4,767,704; 4,657,866; 4,927,762; 4,560,655; or 5,122,469; WO 90/03430; WO 87/00195; or U.S. Patent Re. 30,985 may be used as culture media for the

host cells. Any of these media may be supplemented as necessary with hormones and/or other growth factors (such as insulin, transferrin, or epidermal growth factor), salts (such as sodium chloride, calcium, magnesium, and phosphate), buffers (such as HEPES), nucleotides (such as adenosine and thymidine), antibiotics (such as GENTAMYCIN™ drug), trace elements (defined as inorganic compounds usually present at final concentrations in the micromolar range), and glucose or an equivalent energy source. Any other necessary supplements may also be included at appropriate concentrations that would be known to those skilled in the art. The culture conditions, such as temperature, pH, and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan.

5. Detecting Gene Amplification/Expression

Gene amplification and/or expression may be measured in a sample directly, for example, by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, *Proc. Natl. Acad. Sci. USA*, 77:5201-5205 (1980)], dot blotting (DNA analysis), or in situ hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence TAHO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to TAHO DNA and encoding a specific antibody epitope.

6. Purification of Anti-TAHO Antibody and TAHO Polypeptide

Forms of anti-TAHO antibody and TAHO polypeptide may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage. Cells employed in expression of anti-TAHO antibody and TAHO polypeptide can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

It may be desired to purify anti-TAHO antibody and TAHO polypeptide from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns to bind epitope-tagged forms of the anti-TAHO antibody and TAHO polypeptide. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, *Methods in Enzymology* 182 (1990); Scopes *Protein Purification: Principles and Practice*, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for

example, on the nature of the production process used and the particular anti-TAHO antibody or TAHO polypeptide produced.

When using recombinant techniques, the antibody can be produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the antibody is produced intracellularly, as a first step, the particulate debris, either host cells or lysed fragments, are removed, for example, by centrifugation or ultrafiltration. Carter et al., *Bio/Technology* 10:163-167 (1992) describe a procedure for isolating antibodies which are secreted to the periplasmic space of *E. coli*. Briefly, cell paste is thawed in the presence of sodium acetate (pH 3.5), EDTA, and phenylmethylsulfonyl fluoride (PMSF) over about 30 min. Cell debris can be removed by centrifugation. Where the antibody is secreted into the medium, supernatants from such expression systems are generally first concentrated using a commercially available protein concentration filter, for example, an Amicon or Millipore Pellicon ultrafiltration unit. A protease inhibitor such as PMSF may be included in any of the foregoing steps to inhibit proteolysis and antibiotics may be included to prevent the growth of adventitious contaminants.

The antibody composition prepared from the cells can be purified using, for example, hydroxylapatite chromatography, gel electrophoresis, dialysis, and affinity chromatography, with affinity chromatography being the preferred purification technique. The suitability of protein A as an affinity ligand depends on the species and isotype of any immunoglobulin Fc domain that is present in the antibody. Protein A can be used to purify antibodies that are based on human $\gamma 1$, $\gamma 2$ or $\gamma 4$ heavy chains (Lindmark et al., *J. Immunol. Meth.* 62:1-13 (1983)). Protein G is recommended for all mouse isotypes and for human $\gamma 3$ (Guss et al., *EMBO J.* 5:15671575 (1986)). The matrix to which the affinity ligand is attached is most often agarose, but other matrices are available. Mechanically stable matrices such as controlled pore glass or poly(styrene-divinyl)benzene allow for faster flow rates and shorter processing times than can be achieved with agarose. Where the antibody comprises a C_H3 domain, the Bakerbond ABX™ resin (J. T. Baker, Phillipsburg, N.J.) is useful for purification. Other techniques for protein purification such as fractionation on an ion-exchange column, ethanol precipitation, Reverse Phase HPLC, chromatography on silica, chromatography on heparin SEPHAROSE™ chromatography on an anion or cation exchange resin (such as a polyaspartic acid column), chromatofocusing, SDS-PAGE, and ammonium sulfate precipitation are also available depending on the antibody to be recovered.

Following any preliminary purification step(s), the mixture comprising the antibody of interest and contaminants may be subjected to low pH hydrophobic interaction chromatography using an elution buffer at a pH between about 2.5-4.5, preferably performed at low salt concentrations (e.g., from about 0-0.25M salt).

J. Pharmaceutical Formulations

Therapeutic formulations of the anti-TAHO antibodies, TAHO binding oligopeptides, TAHO binding organic molecules and/or TAHO polypeptides used in accordance with the present invention are prepared for storage by mixing the antibody, polypeptide, oligopeptide or organic molecule having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizer *Remington's Pharmaceutical Sciences* 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as acetate, Tris, phosphate, citrate, and

other organic acids; antioxidants including ascorbic-acid and methionine; preservatives (such as octadecyltrimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride; benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; tonics such as trehalose and sodium chloride; sugars such as sucrose, mannitol, trehalose or sorbitol; surfactant such as polysorbate; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEEN®, PLURONICS® or polyethylene glycol (PEG). The antibody preferably comprises the antibody at a concentration of between 5-200 mg/ml, preferably between 10-100 mg/ml.

The formulations herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. For example, in addition to an anti-TAHO antibody, TAHO binding oligopeptide, or TAHO binding organic molecule, it may be desirable to include in the one formulation, an additional antibody, e.g., a second anti-TAHO antibody which binds a different epitope on the TAHO polypeptide, or an antibody to some other target such as a growth factor that affects the growth of the particular cancer. Alternatively, or additionally, the composition may further comprise a chemotherapeutic agent, cytotoxic agent, cytokine, growth inhibitory agent, anti-hormonal agent, and/or cardioprotectant. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in *Remington's Pharmaceutical Sciences*, 16th edition, Osol, A. Ed. (1980).

Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semi-permeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT® (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid.

The formulations to be used for in vivo administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

K. Treatment with Anti-TAHO Antibodies, TAHO Binding Oligopeptides and TAHO Binding Organic Molecules

To determine TAHO expression in the cancer, various detection assays are available. In one embodiment, TAHO

polypeptide overexpression may be analyzed by immunohistochemistry (IHC). Paraffin embedded tissue sections from a tumor biopsy may be subjected to the IHC assay and accorded a TAHO protein staining intensity criteria as follows:

Score 0—no staining is observed or membrane staining is observed in less than 10% of tumor cells.

Score 1+—a faint/barely perceptible membrane staining is detected in more than 10% of the tumor cells. The cells are only stained in part of their membrane.

Score 2+—a weak to moderate complete membrane staining is observed in more than 10% of the tumor cells.

Score 3+—a moderate to strong complete membrane staining is observed in more than 10% of the tumor cells.

Those tumors with 0 or 1+ scores for TAHO polypeptide expression may be characterized as not overexpressing TAHO, whereas those tumors with 2+ or 3+ scores may be characterized as overexpressing TAHO.

Alternatively, or additionally, FISH assays such as the INFORM® (sold by Ventana, Ariz.) or PATHVISION® (Vysis, Ill.) may be carried out on formalin-fixed, paraffin-embedded tumor tissue to determine the extent (if any) of TAHO overexpression in the tumor.

TAHO overexpression or amplification may be evaluated using an *in vivo* detection assay, e.g., by administering a molecule (such as an antibody, oligopeptide or organic molecule) which binds the molecule to be detected and is tagged with a detectable label (e.g., a radioactive isotope or a fluorescent label) and externally scanning the patient for localization of the label.

As described above, the anti-TAHO antibodies, oligopeptides and organic molecules of the invention have various non-therapeutic applications. The anti-TAHO antibodies, oligopeptides and organic molecules of the present invention can be useful for staging of TAHO polypeptide-expressing cancers (e.g., in radioimaging). The antibodies, oligopeptides and organic molecules are also useful for purification or immunoprecipitation of TAHO polypeptide from cells, for detection and quantitation of TAHO polypeptide *in vitro*, e.g., in an ELISA or a Western blot, to kill and eliminate TAHO-expressing cells from a population of mixed cells as a step in the purification of other cells.

Currently, depending on the stage of the cancer, cancer treatment involves one or a combination of the following therapies: surgery to remove the cancerous tissue, radiation therapy, and chemotherapy. Anti-TAHO antibody, oligopeptide or organic molecule therapy may be especially desirable in elderly patients who do not tolerate the toxicity and side effects of chemotherapy well and in metastatic disease where radiation therapy has limited usefulness. The tumor targeting anti-TAHO antibodies, oligopeptides and organic molecules of the invention are useful to alleviate TAHO-expressing cancers upon initial diagnosis of the disease or during relapse. For therapeutic applications, the anti-TAHO antibody, oligopeptide or organic molecule can be used alone, or in combination therapy with, e.g., hormones, antiangiogens, or radiolabelled compounds, or with surgery, cryotherapy, and/or radiotherapy. Anti-TAHO antibody, oligopeptide or organic molecule treatment can be administered in conjunction with other forms of conventional therapy, either consecutively with, pre- or post-conventional therapy. Chemotherapeutic drugs such as TAXOTERE® (docetaxel), TAXOL® (paclitaxel), estramustine and mitoxantrone are used in treating cancer, in particular, in good risk patients. In the present method of the invention for treating or alleviating cancer, the cancer patient can be administered anti-TAHO antibody, oligopeptide or organic molecule in conjunction with treatment with the one or more of the preceding chemotherapeutic

agents. In particular, combination therapy with paclitaxel and modified derivatives (see, e.g., EP0600517) is contemplated. The anti-TAHO antibody, oligopeptide or organic molecule will be administered with a therapeutically effective dose of the chemotherapeutic agent. In another embodiment, the anti-TAHO antibody, oligopeptide or organic molecule is administered in conjunction with chemotherapy to enhance the activity and efficacy of the chemotherapeutic agent, e.g., paclitaxel. The Physicians' Desk Reference (PDR) discloses dosages of these agents that have been used in treatment of various cancers. The dosing regimen and dosages of these aforementioned chemotherapeutic drugs that are therapeutically effective will depend on the particular cancer being treated, the extent of the disease and other factors familiar to the physician of skill in the art and can be determined by the physician.

In one particular embodiment, a conjugate comprising an anti-TAHO antibody, oligopeptide or organic molecule conjugated with a cytotoxic agent is administered to the patient. Preferably, the immunoconjugate bound to the TAHO protein is internalized by the cell, resulting in increased therapeutic efficacy of the immunoconjugate in killing the cancer cell to which it binds. In a preferred embodiment, the cytotoxic agent targets or interferes with the nucleic acid in the cancer cell. Examples of such cytotoxic agents are described above and include maytansinoids, calicheamicins, ribonucleases and DNA endonucleases.

The anti-TAHO antibodies, oligopeptides, organic molecules or toxin conjugates thereof are administered to a human patient, in accord with known methods, such as intravenous administration, e.g., as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intracerebrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation routes. Intravenous or subcutaneous administration of the antibody, oligopeptide or organic molecule is preferred.

Other therapeutic regimens may be combined with the administration of the anti-TAHO antibody, oligopeptide or organic molecule. The combined administration includes co-administration, using separate formulations or a single pharmaceutical formulation, and consecutive administration in either order, wherein preferably there is a time period while both (or all) active agents simultaneously exert their biological activities. Preferably such combined therapy results in a synergistic therapeutic effect.

It may also be desirable to combine administration of the anti-TAHO antibody or antibodies, oligopeptides or organic molecules, with administration of an antibody directed against another tumor antigen associated with the particular cancer.

In another embodiment, the therapeutic treatment methods of the present invention involves the combined administration of an anti-TAHO antibody (or antibodies), oligopeptides or organic molecules and one or more chemotherapeutic agents or growth inhibitory agents, including co-administration of cocktails of different chemotherapeutic agents. Chemotherapeutic agents include estramustine phosphate, prednimustine, cisplatin, 5-fluorouracil, melphalan, cyclophosphamide, hydroxyurea and hydroxyureataxanes (such as paclitaxel and doxorubicin) and/or anthracycline antibiotics. Preparation and dosing schedules for such chemotherapeutic agents may be used according to manufacturers' instructions or as determined empirically by the skilled practitioner. Preparation and dosing schedules for such chemotherapy are also described in Chemotherapy Service Ed., M. C. Perry, Williams & Wilkins, Baltimore, Md. (1992).

The antibody, oligopeptide or organic molecule may be combined with an anti-hormonal compound; e.g., an anti-estrogen compound such as tamoxifen; an anti-progesterone such as onapristone (see, EP 616 812); or an anti-androgen such as flutamide, in dosages known for such molecules. Where the cancer to be treated is androgen independent cancer, the patient may previously have been subjected to anti-androgen therapy and, after the cancer becomes androgen independent, the anti-TAHO antibody, oligopeptide or organic molecule (and optionally other agents as described herein) may be administered to the patient.

Sometimes, it may be beneficial to also co-administer a cardioprotectant (to prevent or reduce myocardial dysfunction associated with the therapy) or one or more cytokines to the patient. In addition to the above therapeutic regimes, the patient may be subjected to surgical removal of cancer cells and/or radiation therapy, before, simultaneously with, or post antibody, oligopeptide or organic molecule therapy. Suitable dosages for any of the above co-administered agents are those presently used and may be lowered due to the combined action (synergy) of the agent and anti-TAHO antibody, oligopeptide or organic molecule.

For the prevention or treatment of disease, the dosage and mode of administration will be chosen by the physician according to known criteria. The appropriate dosage of antibody, oligopeptide or organic molecule will depend on the type of disease to be treated, as defined above, the severity and course of the disease, whether the antibody, oligopeptide or organic molecule is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to the antibody, oligopeptide or organic molecule, and the discretion of the attending physician. The antibody, oligopeptide or organic molecule is suitably administered to the patient at one time or over a series of treatments. Preferably, the antibody, oligopeptide or organic molecule is administered by intravenous infusion or by subcutaneous injections. Depending on the type and severity of the disease, about 1 µg/kg to about 50 mg/kg body weight (e.g., about 0.1-15 mg/kg/dose) of antibody can be an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. A dosing regimen can comprise administering an initial loading dose of about 4 mg/kg, followed by a weekly maintenance dose of about 2 mg/kg of the anti-TAHO antibody. However, other dosage regimens may be useful. A typical daily dosage might range from about µg/kg to 100 mg/kg or more, depending on the factors mentioned above. For repeated administrations over several days or longer, depending on the condition, the treatment is sustained until a desired suppression of disease symptoms occurs. The progress of this therapy can be readily monitored by conventional methods and assays and based on criteria known to the physician or other persons of skill in the art.

Aside from administration of the antibody protein to the patient, the present application contemplates administration of the antibody by gene therapy. Such administration of nucleic acid encoding the antibody is encompassed by the expression "administering a therapeutically effective amount of an antibody". See, for example, WO96/07321 published Mar. 14, 1996 concerning the use of gene therapy to generate intracellular antibodies.

There are two major approaches to getting the nucleic acid (optionally contained in a vector) into the patient's cells; in vivo and ex vivo. For in vivo delivery the nucleic acid is injected directly into the patient, usually at the site where the antibody is required. For ex vivo treatment, the patient's cells are removed, the nucleic acid is introduced into these isolated

cells and the modified cells are administered to the patient either directly or, for example, encapsulated within porous membranes which are implanted into the patient (see, e.g., U.S. Pat. Nos. 4,892,538 and 5,283,187). There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells in vitro, or in vivo in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells in vitro include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. A commonly used vector for ex vivo delivery of the gene is a retroviral vector.

The currently preferred in vivo nucleic acid transfer techniques include transfection with viral vectors (such as adenovirus, Herpes simplex I virus, or adeno-associated virus) and lipid-based systems (useful lipids for lipid-mediated transfer of the gene are DOTMA, DOPE and DC-Chol, for example). For review of the currently known gene marking and gene therapy protocols see Anderson et al., *Science* 256:808-813 (1992). See also WO 93/25673 and the references cited therein.

The anti-TAHO antibodies of the invention can be in the different forms encompassed by the definition of "antibody" herein. Thus, the antibodies include full length or intact antibody, antibody fragments, native sequence antibody or amino acid variants, humanized, chimeric or fusion antibodies, immunoconjugates, and functional fragments thereof. In fusion antibodies an antibody sequence is fused to a heterologous polypeptide sequence. The antibodies can be modified in the Fc region to provide desired effector functions. As discussed in more detail in the sections herein, with the appropriate Fc regions, the naked antibody bound on the cell surface can induce cytotoxicity, e.g., via antibody-dependent cellular cytotoxicity (ADCC) or by recruiting complement in complement dependent cytotoxicity, or some other mechanism. Alternatively, where it is desirable to eliminate or reduce effector function, so as to minimize side effects or therapeutic complications, certain other Fc regions may be used.

In one embodiment, the antibody competes for binding or bind substantially to, the same epitope as the antibodies of the invention. Antibodies having the biological characteristics of the present anti-TAHO antibodies of the invention are also contemplated, specifically including the in vivo tumor targeting and any cell proliferation inhibition or cytotoxic characteristics.

Methods of producing the above antibodies are described in detail herein.

The present anti-TAHO antibodies, oligopeptides and organic molecules are useful for treating a TAHO-expressing cancer or alleviating one or more symptoms of the cancer in a mammal. Such a cancer includes, but is not limited to, hematopoietic cancers or blood-related cancers, such as lymphoma, leukemia, myeloma or lymphoid malignancies, but also cancers of the spleen and cancers of the lymph nodes. More particular examples of such B-cell associated cancers, including for example, high, intermediate and low grade lymphomas (including B cell lymphomas such as, for example, mucosa-associated-lymphoid tissue B cell lymphoma and non-Hodgkin's lymphoma, mantle cell lymphoma, Burkitt's lymphoma, small lymphocytic lymphoma, marginal zone lymphoma, diffuse large cell lymphoma, follicular lymphoma, and Hodgkin's lymphoma and T cell lymphomas) and leukemias (including secondary leukemia, chronic lymphocytic leukemia, such as B cell leukemia (CD5+ B lymphocytes), myeloid leukemia, such as acute myeloid leuke-

mia, chronic myeloid leukemia, lymphoid leukemia, such as acute lymphoblastic leukemia and myelodysplasia), multiple myeloma, such as plasma cell malignancy, and other hematological and/or B cell- or T-cell-associated cancers. The cancers encompass metastatic cancers of any of the preceding. The antibody, oligopeptide or organic molecule is able to bind to at least a portion of the cancer cells that express TAHO polypeptide in the mammal. In a preferred embodiment, the antibody, oligopeptide or organic molecule is effective to destroy or kill TAHO-expressing tumor cells or inhibit the growth of such tumor cells, *in vitro* or *in vivo*, upon binding to TAHO polypeptide on the cell. Such an antibody includes a naked anti-TAHO antibody (not conjugated to any agent). Naked antibodies that have cytotoxic or cell growth inhibition properties can be further harnessed with a cytotoxic agent to render them even more potent in tumor cell destruction. Cytotoxic properties can be conferred to an anti-TAHO antibody by, e.g., conjugating the antibody with a cytotoxic agent, to form an immunoconjugate as described herein. The cytotoxic agent or a growth inhibitory agent is preferably a small molecule. Toxins such as calicheamicin or a maytansinoid and analogs or derivatives thereof, are preferable.

The invention provides a composition comprising an anti-TAHO antibody, oligopeptide or organic molecule of the invention, and a carrier. For the purposes of treating cancer, compositions can be administered to the patient in need of such treatment, wherein the composition can comprise one or more anti-TAHO antibodies present as an immunoconjugate or as the naked antibody. In a further embodiment, the compositions can comprise these antibodies, oligopeptides or organic molecules in combination with other therapeutic agents such as cytotoxic or growth inhibitory agents, including chemotherapeutic agents. The invention also provides formulations comprising an anti-TAHO antibody, oligopeptide or organic molecule of the invention, and a carrier. In one embodiment, the formulation is a therapeutic formulation comprising a pharmaceutically acceptable carrier.

Another aspect of the invention is isolated nucleic acids encoding the anti-TAHO antibodies. Nucleic acids encoding both the H and L chains and especially the hypervariable region residues, chains which encode the native sequence antibody as well as variants, modifications and humanized versions of the antibody, are encompassed.

The invention also provides methods useful for treating a TAHO polypeptide-expressing cancer or alleviating one or more symptoms of the cancer in a mammal, comprising administering a therapeutically effective amount of an anti-TAHO antibody, oligopeptide or organic molecule to the mammal. The antibody, oligopeptide or organic molecule therapeutic compositions can be administered short term (acute) or chronic, or intermittent as directed by physician. Also provided are methods of inhibiting the growth of, and killing a TAHO polypeptide-expressing cell.

The invention also provides kits and articles of manufacture comprising at least one anti-TAHO antibody, oligopeptide or organic molecule. Kits containing anti-TAHO antibodies, oligopeptides or organic molecules find use, e.g., for TAHO cell killing assays, for purification or immunoprecipitation of TAHO polypeptide from cells. For example, for isolation and purification of TAHO, the kit can contain an anti-TAHO antibody, oligopeptide or organic molecule coupled to beads (e.g., sepharose beads). Kits can be provided which contain the antibodies, oligopeptides or organic molecules for detection and quantitation of TAHO *in vitro*, e.g., in an ELISA or a Western blot. Such antibody, oligopeptide or organic molecule useful for detection may be provided with a label such as a fluorescent or radiolabel.

L. Articles of Manufacture and Kits

Another embodiment of the invention is an article of manufacture containing materials useful for the treatment of anti-TAHO expressing cancer. The article of manufacture comprises a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials, syringes, etc. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition which is effective for treating the cancer condition and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). At least one active agent in the composition is an anti-TAHO antibody, oligopeptide or organic molecule of the invention. The label or package insert indicates that the composition is used for treating cancer. The label or package insert will further comprise instructions for administering the antibody, oligopeptide or organic molecule composition to the cancer patient. Additionally, the article of manufacture may further comprise a second container comprising a pharmaceutically-acceptable buffer, such as bacteriostatic water for injection (BWFI), phosphate-buffered saline, Ringer's solution and dextrose solution. It may further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, and syringes.

Kits are also provided that are useful for various purposes, e.g., for TAHO-expressing cell killing assays, for purification or immunoprecipitation of TAHO polypeptide from cells. For isolation and purification of TAHO polypeptide, the kit can contain an anti-TAHO antibody, oligopeptide or organic molecule coupled to beads (e.g., sepharose beads). Kits can be provided which contain the antibodies, oligopeptides or organic molecules for detection and quantitation of TAHO polypeptide *in vitro*, e.g., in an ELISA or a Western blot. As with the article of manufacture, the kit comprises a container and a label or package insert on or associated with the container. The container holds a composition comprising at least one anti-TAHO antibody, oligopeptide or organic molecule of the invention. Additional containers may be included that contain, e.g., diluents and buffers, control antibodies. The label or package insert may provide a description of the composition as well as instructions for the intended *in vitro* or detection use.

M. Uses for TAHO Polypeptides and TAHO-Polypeptide Encoding Nucleic Acids

Nucleotide sequences (or their complement) encoding TAHO polypeptides have various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA probes. TAHO-encoding nucleic acid will also be useful for the preparation of TAHO polypeptides by the recombinant techniques described herein, wherein those TAHO polypeptides may find use, for example, in the preparation of anti-TAHO antibodies as described herein.

The full-length native sequence TAHO gene, or portions thereof, may be used as hybridization probes for a cDNA library to isolate the full-length TAHO cDNA or to isolate still other cDNAs (for instance, those encoding naturally-occurring variants of TAHO or TAHO from other species) which have a desired sequence identity to the native TAHO sequence disclosed herein. Optionally, the length of the probes will be about 20 to about 50 bases. The hybridization probes may be derived from at least partially novel regions of the full length native nucleotide sequence wherein those regions may be determined without undue experimentation or from genomic

sequences including promoters, enhancer elements and introns of native sequence TAHO. By way of example, a screening method will comprise isolating the coding region of the TAHO gene using the known DNA sequence to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels, including radionucleotides such as ³²P or ³⁵S, or enzymatic labels such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems. Labeled probes having a sequence complementary to that of the TAHO gene of the present invention can be used to screen libraries of human cDNA, genomic DNA or mRNA to determine which members of such libraries the probe hybridizes to. Hybridization techniques are described in further detail in the Examples below. Any EST sequences disclosed in the present application may similarly be employed as probes, using the methods disclosed herein.

Other useful fragments of the TAHO-encoding nucleic acids include antisense or sense oligonucleotides comprising a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target TAHO mRNA (sense) or TAHO DNA (antisense) sequences. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment of the coding region of TAHO DNA: Such a fragment generally comprises at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (*Cancer Res.* 48:2659, 1988) and van der Krol et al. (*BioTechniques* 6:958, 1988).

Binding of antisense or sense oligonucleotides to target nucleic acid sequences results in the formation of duplexes that block transcription or translation of the target sequence by one of several means, including enhanced degradation of the duplexes, premature termination of transcription or translation, or by other means. Such methods are encompassed by the present invention. The antisense oligonucleotides thus may be used to block expression of TAHO proteins, wherein those TAHO proteins may play a role in the induction of cancer in mammals. Antisense or sense oligonucleotides further comprise oligonucleotides having modified sugar-phosphodiester backbones (or other sugar linkages, such as those described in WO 91/06629) and wherein such sugar linkages are resistant to endogenous nucleases. Such oligonucleotides with resistant sugar linkages are stable in vivo (i.e., capable of resisting enzymatic degradation) but retain sequence specificity to be able to bind to target nucleotide sequences.

Preferred intragenic sites for antisense binding include the region incorporating the translation initiation/start codon (5'-AUG/5'-ATG) or termination/stop codon (5'-UAA, 5'-UAG and 5'-UGA/5'-TAA, 5'-TAG and 5'-TGA) of the open reading frame (ORF) of the gene. These regions refer to a portion of the mRNA or gene that encompasses from about 25 to about 50 contiguous nucleotides in either direction (i.e., 5' or 3') from a translation initiation or termination codon. Other preferred regions for antisense binding include: introns; exons; intron-exon junctions; the open reading frame (ORF) or "coding region," which is the region between the translation initiation codon and the translation termination codon; the 5' cap of an mRNA which comprises an N7-methylated guanosine residue joined to the 5'-most residue of the mRNA via a 5'-5' triphosphate linkage and includes 5' cap structure itself as well as the first 50 nucleotides adjacent to the cap; the 5' untranslated region (5'UTR), the portion of an mRNA in the 5' direction from the translation initiation codon, and thus including nucleotides between the 5' cap site and the translation initiation codon of an mRNA or corresponding nucleotides on the gene; and the 3' untranslated region (3'UTR), the

portion of an mRNA in the 3' direction from the translation termination codon, and thus including nucleotides between the translation termination codon and 3' end of an mRNA or corresponding nucleotides on the gene.

Specific examples of preferred antisense compounds useful for inhibiting expression of TAHO proteins include oligonucleotides containing modified backbones or non-natural internucleoside linkages. Oligonucleotides having modified backbones include those that retain a phosphorus atom in the backbone and those that do not have a phosphorus atom in the backbone. For the purposes of this specification, and as sometimes referenced in the art, modified oligonucleotides that do not have a phosphorus atom in their internucleoside backbone can also be considered to be oligonucleosides. Preferred modified oligonucleotide backbones include, for example, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotri-esters, methyl and other alkyl phosphonates including 3'-alkylene phosphonates, 5'-alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thiono phosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, selenophosphates and borano-phosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity wherein one or more internucleotide linkages is a 3' to 3', 5' to 5' or 2' to 2' linkage. Preferred oligonucleotides having inverted polarity comprise a single 3' to 3' linkage at the 3'-most internucleotide linkage i.e. a single inverted nucleoside residue which may be abasic (the nucleobase is missing or has a hydroxyl group in place thereof). Various salts, mixed salts and free acid forms are also included. Representative United States patents that teach the preparation of phosphorus-containing linkages include, but are not limited to, U.S. Pat. Nos. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5,177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,306; 5,550,111; 5,563,253; 5,571,799; 5,587,361; 5,194,599; 5,565,555; 5,527,899; 5,721,218; 5,672,697 and 5,625,050, each of which is herein incorporated by reference.

Preferred modified oligonucleotide backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; riboacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH.sub.2 component parts. Representative United States patents that teach the preparation of such oligonucleosides include, but are not limited to, U.S. Pat. Nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437; 5,792,608; 5,646,269 and 5,677,439, each of which is herein incorporated by reference.

In other preferred antisense oligonucleotides, both the sugar and the internucleoside linkage, i.e., the backbone, of

the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound. One such oligomeric compound, an oligonucleotide mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar-backbone of an oligonucleotide is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleobases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone. Representative United States patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Pat. Nos. 5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference. Further teaching of PNA compounds can be found in Nielsen et al., *Science*, 1991, 254, 1497-1500.

Preferred antisense oligonucleotides incorporate phosphorothioate backbones and/or heteroatom backbones, and in particular $-\text{CH}_2-\text{NH}-\text{O}-\text{CH}_2-$, $-\text{CH}_2-\text{N}(\text{CH}_3)-\text{O}-\text{CH}_2-$ [known as a methylene (methylimino) or MMI backbone], $-\text{CH}_2-\text{O}-\text{N}(\text{CH}_3)-\text{CH}_2-$, $-\text{CH}_2-\text{N}(\text{CH}_3)-\text{N}(\text{CH}_3)-\text{CH}_2-$ and $-\text{O}-\text{N}(\text{C}_3)-\text{CH}_2-\text{CH}_2-$ [wherein the native phosphodiester backbone is represented as $-\text{O}-\text{P}-\text{O}-\text{CH}_2-$] described in the above referenced U.S. Pat. No. 5,489,677, and the amide backbones of the above referenced U.S. Pat. No. 5,602,240. Also preferred are antisense oligonucleotides having morpholino backbone structures of the above-referenced U.S. Pat. No. 5,034,506.

Modified oligonucleotides may also contain one or more substituted sugar moieties. Preferred oligonucleotides comprise one of the following at the 2' position: OH; F; O-alkyl, S-alkyl, or N-alkyl; O-alkenyl, S-alkenyl, or N-alkenyl; O-alkynyl, S-alkynyl or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted C_1 to C_{10} alkyl or C_2 to C_{10} alkenyl and alkynyl. Particularly preferred are $\text{O}[(\text{CH}_2)_n\text{O}]_m\text{CH}_3$, $\text{O}(\text{CH}_2)_n\text{OCH}_3$, $\text{O}(\text{CH}_2)_n\text{NH}_2$, $\text{O}(\text{CH}_2)_n\text{CH}_3$, $\text{O}(\text{CH}_2)_n\text{ONH}_2$, and $\text{O}(\text{CH}_2)_n\text{ON}[(\text{CH}_2)_m\text{CH}_3]_2$, where n and m are from 1 to about 10. Other preferred antisense oligonucleotides comprise one of the following at the 2' position: C_1 to C_{10} lower alkyl, substituted lower alkyl, alkenyl, alkynyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH_3 , OCN , Cl, Br, CN, CF_3 , OCF_3 , SOCH_3 , SO_2CH_3 , ONO_2 , NO_2 , N_3 , NH_2 , heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an intercalator, a group for improving the pharmacokinetic properties of an oligonucleotide, or a group for improving the pharmacodynamic properties of an oligonucleotide, and other substituents having similar properties. A preferred modification includes 2'-methoxyethoxy (2'-O- $\text{CH}_2\text{CH}_2\text{OCH}_3$, also known as 2'-O-(2-methoxyethyl) or 2'-MOE) (Martin et al., *Helv. Chim. Acta*, 1995, 78, 486-504) i.e., an alkoxyalkoxy group. A further preferred modification includes 2'-dimethylaminoethoxy, i.e., a $\text{O}(\text{CH}_2)_2\text{ON}(\text{CH}_3)_2$ group, also known as 2'-DMAOE, as described in examples hereinbelow, and 2'-dimethylaminoethoxyethyl (also known in the art as 2'-O-dimethylaminoethoxyethyl or 2'-DMAEOE), i.e., 2'-O- $\text{CH}_2-\text{O}-\text{CH}_2-\text{N}(\text{CH}_2)$.

A further preferred modification includes Locked Nucleic Acids (LNAs) in which the 2'-hydroxyl group is linked to the 3' or 4' carbon atom of the sugar ring thereby forming a bicyclic sugar moiety. The linkage is preferably a methylene ($-\text{CH}_2-$)_n group bridging the 2' oxygen atom and the 4' carbon atom wherein n is 1 or 2. LNAs and preparation thereof are described in WO 98/39352 and WO 99/14226.

Other preferred modifications include 2'-methoxy (2'-O- CH_3), 2'-aminopropoxy (2'-O- $\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$), 2'-allyl (2'-

$\text{CH}_2-\text{CH}=\text{CH}_2$), 2'-O-allyl (2'-O- $\text{CH}_2-\text{CH}=\text{CH}_2$) and 2'-fluoro (2'-F). The 2'-modification may be in the arabino (up) position or ribo (down) position. A preferred 2'-arabino modification is 2'-F. Similar modifications may also be made at other positions on the oligonucleotide, particularly the 3' position of the sugar on the 3' terminal nucleotide or in 2'-5' linked oligonucleotides and the 5' position of 5' terminal nucleotide. Oligonucleotides may also have sugar mimetics such as cyclobutyl moieties in place of the pentofuranosyl sugar. Representative United States patents that teach the preparation of such modified sugar structures include, but are not limited to, U.S. Pat. Nos. 4,981,957; 5,118,800; 5,319,080; 5,359,044; 5,393,878; 5,446,137; 5,466,786; 5,514,785; 5,519,134; 5,567,811; 5,576,427; 5,591,722; 5,597,909; 5,610,300; 5,627,053; 5,639,873; 5,646,265; 5,658,873; 5,670,633; 5,792,747; and 5,700,920, each of which is herein incorporated by reference in its entirety.

Oligonucleotides may also include nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). Modified nucleobases include other synthetic and natural nucleobases such as 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl ($-\text{C}\equiv\text{C}-\text{CH}_3$ or $-\text{CH}_2-\text{C}\equiv\text{CH}$) uracil and cytosine and other alkynyl derivatives of pyrimidine bases, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine and 7-methyladenine, 2-F-adenine, 2-amino-adenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3-deazaguanine and 3-deazaadenine. Further modified nucleobases include tricyclic pyrimidines such as phenoxazine cytidine (1H-pyrimido [5,4-b][1,4]benzoxazin-2(3H)-one), phenothiazine cytidine (1H-pyrimido[5,4-b][1,4]benzothiazin-2(3H)-one),

G-clamps such as a substituted phenoxazine cytidine (e.g. 9-(2-aminoethoxy)-H-pyrimido[5,4-b][1,4]benzoxazin-2(3H)-one), carbazole cytidine (2H-pyrimido[4,5-b]indol-2-one), pyridoindole cytidine (H-pyrido[3',2':4,5]pyrrolo[2,3-d]pyrimidin-2-one). Modified nucleobases may also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Further nucleobases include those disclosed in U.S. Pat. No. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, pages 858-859, Kroschwitz, J. I., ed. John Wiley & Sons, 1990, and those disclosed by Englisch et al., *Angewandte Chemie, International Edition*, 1991, 30, 613. Certain of these nucleobases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and O-6 substituted purines, including 2-aminopropyladenine, 5-propynyluracil and 5-propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2.degree. C. (Sanghvi et al, *Antisense Research and Applications*, CRC Press, Boca Raton, 1993, pp. 276-278) and are preferred base substitutions, even more particularly when combined with 2'-O-methoxyethyl sugar modifications. Representative United States patents that teach the preparation of

modified nucleobases include, but are not limited to: U.S. Pat. No. 3,687,808, as well as U.S. Pat. Nos. 4,845,205; 5,130,302; 5,134,066; 5,175,273; 5,367,066; 5,432,272; 5,457,187; 5,459,255; 5,484,908; 5,502,177; 5,525,711; 5,552,540; 5,587,469; 5,594,121; 5,596,091; 5,614,617; 5,645,985; 5,830,653; 5,763,588; 6,005,096; 5,681,941 and 5,750,692, each of which is herein incorporated by reference.

Another modification of antisense oligonucleotides chemically linking to the oligonucleotide one or more moieties or conjugates which enhance the activity, cellular distribution or cellular uptake of the oligonucleotide. The compounds of the invention can include conjugate groups covalently bound to functional groups such as primary or secondary hydroxyl groups. Conjugate groups of the invention include intercalators, reporter molecules, polyamines, polyamides, polyethylene glycols, polyethers, groups that enhance the pharmacodynamic properties of oligomers, and groups that enhance the pharmacokinetic properties of oligomers. Typical conjugate groups include cholesterol, lipids, cation lipids, phospholipids, cationic phospholipids, biotin, phenazine, folate, phenanthridine, anthraquinone, acridine, fluoresceins, rhodamines, coumarins, and dyes. Groups that enhance the pharmacodynamic properties, in the context of this invention, include groups that improve oligomer uptake, enhance oligomer resistance to degradation, and/or strengthen sequence-specific hybridization with RNA. Groups that enhance the pharmacokinetic properties, in the context of this invention, include groups that improve oligomer uptake, distribution, metabolism or excretion. Conjugate moieties include but are not limited to lipid moieties such as a cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86, 6553-6556), cholic acid (Manoharan et al., Bioorg. Med. Chem. Lett., 1994, 4, 1053-1060), a thioether, e.g., hexyl-5-tritylthiol (Manoharan et al., Ann. N.Y. Acad. Sci., 1992, 660, 306-309; Manoharan et al., Bioorg. Med. Chem. Lett., 1993, 3, 2765-2770), a thiocholesterol (Oberhauser et al., Nucl. Acids Res., 1992, 20, 533-538), an aliphatic chain, e.g., dodecandiol or undecyl residues (Saison-Behmoaras et al., EMBO J., 1991, 10, 1111-1118; Kabanov et al., FEBS Lett., 1990, 259, 327-330; Svinarchuk et al., Biochimie, 1993, 75, 49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., Tetrahedron Lett., 1995, 36, 3651-3654; Shea et al., Nucl. Acids Res., 1990, 18, 3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., Nucleosides & Nucleotides, 1995, 14, 969-973), or adamantane acetic acid (Manoharan et al., Tetrahedron Lett., 1995, 36, 3651-3654), a palmityl moiety (Mishra et al., Biochim. Biophys. Acta, 1995, 1264, 229-237), or an octadecylamine or hexylamino-carbonyl-oxysterol moiety. Oligonucleotides of the invention may also be conjugated to active drug substances, for example, aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, carprofen, dansylsarcosine, 2,3,5-triodobenzoic acid, flufenamic acid, folinic acid, a benzothiadiazide, chlorothiazide, a diazepam, indomethacin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic. Oligonucleotide-drug conjugates and their preparation are described in U.S. patent application Ser. No. 09/334,130 (filed Jun. 15, 1999) and U.S. Pat. Nos. 4,828,979; 4,948,882; 5,218,105; 5,525,465; 5,541,313; 5,545,730; 5,552,538; 5,578,717; 5,580,731; 5,580,731; 5,591,584; 5,109,124; 5,118,802; 5,138,045; 5,414,077; 5,486,603; 5,512,439; 5,578,718; 5,608,046; 4,587,044; 4,605,735; 4,667,025; 4,762,779; 4,789,737; 4,824,941; 4,835,263; 4,876,335; 4,904,582; 4,958,013; 5,082,830; 5,112,963; 5,214,136; 5,082,830; 5,112,963; 5,214,136; 5,245,022;

5,254,469; 5,258,506; 5,262,536; 5,272,250; 5,292,873; 5,317,098; 5,371,241; 5,391,723; 5,416,203; 5,451,463; 5,510,475; 5,512,667; 5,514,785; 5,565,552; 5,567,810; 5,574,142; 5,585,481; 5,587,371; 5,595,726; 5,597,696; 5,599,923; 5,599,928 and 5,688,941, each of which is herein incorporated by reference.

It is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications may be incorporated in a single compound or even at a single nucleoside within an oligonucleotide. The present invention also includes antisense compounds which are chimeric compounds. "Chimeric" antisense compounds or "chimeras," in the context of this invention, are antisense compounds, particularly oligonucleotides, which contain two or more chemically distinct regions, each made up of at least one monomer unit, i.e., a nucleotide in the case of an oligonucleotide compound. These oligonucleotides typically contain at least one region wherein the oligonucleotide is modified so as to confer upon the oligonucleotide increased resistance to nuclease degradation, increased cellular uptake, and/or increased binding affinity for the target nucleic acid. An additional region of the oligonucleotide may serve as a substrate for enzymes capable of cleaving RNA:DNA or RNA:RNA hybrids. By way of example, RNase H is a cellular endonuclease which cleaves the RNA strand of an RNA:DNA duplex. Activation of RNase H, therefore, results in cleavage of the RNA target, thereby greatly enhancing the efficiency of oligonucleotide inhibition of gene expression. Consequently, comparable results can often be obtained with shorter oligonucleotides when chimeric oligonucleotides are used, compared to phosphorothioate deoxyoligonucleotides hybridizing to the same target region. Chimeric antisense compounds of the invention may be formed as composite structures of two or more oligonucleotides, modified oligonucleotides, oligonucleosides and/or oligonucleotide mimetics as described above. Preferred chimeric antisense oligonucleotides incorporate at least one 2' modified sugar (preferably 2'-O-(C₂H₅)₂-O-CH₃) at the 3' terminal to confer nuclease resistance and a region with at least 4 contiguous 2'-H sugars to confer RNase H activity. Such compounds have also been referred to in the art as hybrids or gapmers. Preferred gapmers have a region of 2' modified sugars (preferably 2'-O-(CH₂)₂-O-CH₃) at the 3'-terminal and at the 5' terminal separated by at least one region having at least 4 contiguous 2'-H sugars and preferably incorporate phosphorothioate backbone linkages. Representative United States patents that teach the preparation of such hybrid structures include, but are not limited to, U.S. Pat. Nos. 5,013,830; 5,149,797; 5,220,007; 5,256,775; 5,366,878; 5,403,711; 5,491,133; 5,565,350; 5,623,065; 5,652,355; 5,652,356; and 5,700,922, each of which is herein incorporated by reference in its entirety.

The antisense compounds used in accordance with this invention may be conveniently and routinely made through the well-known technique of solid phase synthesis. Equipment for such synthesis is sold by several vendors including, for example, Applied Biosystems (Foster City, Calif.). Any other means for such synthesis known in the art may additionally or alternatively be employed. It is well known to use similar techniques to prepare oligonucleotides such as the phosphorothioates and alkylated derivatives. The compounds of the invention may also be admixed, encapsulated, conjugated or otherwise associated with other molecules, molecule structures or mixtures of compounds, as for example, liposomes, receptor targeted molecules, oral, rectal, topical or other formulations, for assisting in uptake, distribution and/or absorption. Representative United States patents that teach

the preparation of such uptake, distribution and/or absorption assisting formulations include, but are not limited to, U.S. Pat. Nos. 5,108,921; 5,354,844; 5,416,016; 5,459,127; 5,521,291; 5,543,158; 5,547,932; 5,583,020; 5,591,721; 4,426,330; 4,534,899; 5,013,556; 5,108,921; 5,213,804; 5,227,170; 5,264,221; 5,356,633; 5,395,619; 5,416,016; 5,417,978; 5,462,854; 5,469,854; 5,512,295; 5,527,528; 5,534,259; 5,543,152; 5,556,948; 5,580,575; and 5,595,756, each of which is herein incorporated by reference.

Other examples of sense or antisense oligonucleotides include those oligonucleotides which are covalently linked to organic moieties, such as those described in WO 90/10048, and other moieties that increase affinity of the oligonucleotide for a target nucleic acid sequence, such as poly-(L-lysine). Further still, intercalating agents, such as ellipticine, and alkylating agents or metal complexes may be attached to sense or antisense oligonucleotides to modify binding specificities of the antisense or sense oligonucleotide for the target nucleotide sequence.

Antisense or sense oligonucleotides may be introduced into a cell containing the target nucleic acid sequence by any gene transfer method, including, for example, CaPO₄-mediated DNA transfection, electroporation, or by using gene transfer vectors such as Epstein-Barr virus. In a preferred procedure, an antisense or sense oligonucleotide is inserted into a suitable retroviral vector. A cell containing the target nucleic acid sequence is contacted with the recombinant retroviral vector, either *in vivo* or *ex vivo*. Suitable retroviral vectors include, but are not limited to, those derived from the murine retrovirus M-MuLV, N2 (a retrovirus derived from M-MuLV), or the double copy vectors designated DCT5A, DCT5B and DCT5C (see WO 90/13641).

Sense or antisense oligonucleotides also may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell.

Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. The sense or antisense oligonucleotide-lipid complex is preferably dissociated within the cell by an endogenous lipase.

Antisense or sense RNA or DNA molecules are generally at least about 5 nucleotides in length, alternatively at least about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 610, 620, 630, 640, 650, 660, 670, 680, 690, 700, 710, 720, 730, 740, 750, 760, 770, 780, 790, 800, 810, 820, 830, 840, 850, 860, 870, 880, 890, 900, 910, 920, 930, 940, 950, 960, 970, 980, 990, or 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length.

The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related TAHO coding sequences.

Nucleotide sequences encoding a TAHO can also be used to construct hybridization probes for mapping the gene which encodes that TAHO and for the genetic analysis of individuals with genetic disorders. The nucleotide sequences provided herein may be mapped to a chromosome and specific regions of a chromosome using known techniques, such as *in situ* hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

When the coding sequences for TAHO encode a protein which binds to another protein (example, where the TAHO is a receptor), the TAHO can be used in assays to identify the other proteins or molecules involved in the binding interaction. By such methods, inhibitors of the receptor/ligand binding interaction can be identified. Proteins involved in such binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction. Also, the receptor TAHO can be used to isolate correlative ligand(s). Screening assays can be designed to find lead compounds that mimic the biological activity of a native TAHO or a receptor for TAHO. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art.

Nucleic acids which encode TAHO or its modified forms can also be used to generate either transgenic animals or "knock out" animals which, in turn, are useful in the development and screening of therapeutically useful reagents. A transgenic animal (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prenatal, e.g., an embryonic stage. A transgene is a DNA which is integrated into the genome of a cell from which a transgenic animal develops. In one embodiment, cDNA encoding TAHO can be used to clone genomic DNA encoding TAHO in accordance with established techniques and the genomic sequences used to generate transgenic animals that contain cells which express DNA encoding TAHO. Methods for generating transgenic animals, particularly animals such as mice or rats, have become conventional in the art and are described, for example, in U.S. Pat. Nos. 4,736,866 and 4,870,009. Typically, particular cells would be targeted for TAHO transgene incorporation with tissue-specific enhancers. Transgenic animals that include a copy of a transgene encoding TAHO introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased expression of DNA encoding TAHO. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with this facet of the invention, an animal is treated with the reagent and a reduced incidence of the pathological condition, compared to untreated animals bearing the transgene, would indicate a potential therapeutic intervention for the pathological condition.

Alternatively, non-human homologues of TAHO can be used to construct a TAHO "knock out" animal which has a defective or altered gene encoding TAHO as a result of homologous recombination between the endogenous gene encoding TAHO and altered genomic DNA encoding TAHO

introduced into an embryonic stem cell of the animal. For example, cDNA encoding TAHO can be used to clone genomic DNA encoding TAHO in accordance with established techniques. A portion of the genomic DNA encoding TAHO can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector [see e.g., Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see e.g., Li et al., *Cell*, 69:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (e.g., a mouse or rat) to form aggregation chimeras [see e.g., Bradley, in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend against certain pathological conditions and for their development of pathological conditions due to absence of the TAHO polypeptide.

Nucleic acid encoding the TAHO polypeptides may also be used in gene therapy. In gene therapy applications, genes are introduced into cells in order to achieve in vivo synthesis of a therapeutically effective genetic product, for example for replacement of a defective gene. "Gene therapy" includes both conventional gene therapy where a lasting effect is achieved by a single treatment, and the administration of gene therapeutic agents, which involves the one time or repeated administration of a therapeutically effective DNA or mRNA. Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes in vivo. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik et al., *Proc. Natl. Acad. Sci. USA* 83:4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells in vitro, or in vivo in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells in vitro include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred in vivo gene transfer techniques include transfection with viral (typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau et al., *Trends in Biotechnology* 11, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins

which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu et al., *J. Biol. Chem.* 262, 4429-4432 (1987); and Wagner et al., *Proc. Natl. Acad. Sci. USA* 87, 3410-3414 (1990). For review of gene marking and gene therapy protocols see Anderson et al., *Science* 256, 808-813 (1992).

The nucleic acid molecules encoding the TAHO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each TAHO nucleic acid molecule of the present invention can be used as a chromosome marker.

The TAHO polypeptides and nucleic acid molecules of the present invention may also be used diagnostically for tissue typing, wherein the TAHO polypeptides of the present invention may be differentially expressed in one tissue as compared to another, preferably in a diseased tissue as compared to a normal tissue of the same tissue type. TAHO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis.

This invention encompasses methods of screening compounds to identify those that mimic the TAHO polypeptide (agonists) or prevent the effect of the TAHO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the TAHO polypeptides encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins, including e.g., inhibiting the expression of TAHO polypeptide from cells. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, and cell-based assays, which are well characterized in the art.

All assays for antagonists are common in that they call for contacting the drug candidate with a TAHO polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the TAHO polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the TAHO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monoclonal antibody, specific for the TAHO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complex-

ing can be detected, for example, by using a labeled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular TAHO polypeptide encoded by a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, e.g., cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers (Fields and Song, *Nature (London)*, 340:245-246 (1989); Chien et al., *Proc. Natl. Acad. Sci. USA*, 88:9578-9582 (0.1991)) as disclosed by Chevray and Nathans, *Proc. Natl. Acad. Sci. USA*, 89: 5789-5793 (1991). Many transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, the other one functioning as the transcription-activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-lacZ reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for β -galactosidase. A complete kit (MATCHMAKER™) for identifying protein-protein interactions between two specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

Compounds that interfere with the interaction of a gene encoding a TAHO polypeptide identified herein and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a candidate compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

To assay for antagonists, the TAHO polypeptide may be added to a cell along with the compound to be screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence of the TAHO polypeptide indicates that the compound is an antagonist to the TAHO polypeptide. Alternatively, antagonists may be detected by combining the TAHO polypeptide and a potential antagonist with membrane-bound TAHO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition assay. The TAHO polypeptide can be labeled, such as by radioactivity, such that the number of TAHO polypeptide molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene encoding the receptor can be identified by

numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting. Coligan et al., *Current Protocols in Immun.*, 1(2): Chapter 5 (1991). Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the TAHO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the TAHO polypeptide. Transfected cells that are grown on glass slides are exposed to labeled TAHO polypeptide. The TAHO polypeptide can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a single clone that encodes the putative receptor.

As an alternative approach for receptor identification, labeled TAHO polypeptide can be photoaffinity-linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised, resolved into peptide fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained from micro-sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the gene encoding the putative receptor.

In another assay for antagonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled TAHO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with TAHO polypeptide, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the TAHO polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the TAHO polypeptide.

Another potential TAHO polypeptide antagonist is an antisense RNA or DNA construct prepared using antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used to control gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide sequence, which encodes the mature TAHO polypeptides herein, is used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription (triple helix—see Lee et al., *Nucl. Acids Res.*, 6:3073 (1979); Cooney et al., *Science*, 241: 456 (1988); Dervan et al., *Science*, 251:1360 (1991)), thereby preventing transcription and the production of the TAHO polypeptide. The antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into the TAHO polypeptide (antisense—Okano, *Neurochem.*, 56:560 (1991); *Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression* (CRC

Press: Boca Raton, Fla., 1988). The oligonucleotides described above can also be delivered to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of the TAHO polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiation site, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the TAHO polypeptide, thereby blocking the normal biological activity of the TAHO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and synthetic non-peptidyl organic or inorganic compounds.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, *Current Biology*, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published Sep. 18, 1997).

Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, supra.

These small molecules can be identified by any one or more of the screening assays discussed hereinabove and/or by any other screening techniques well known for those skilled in the art.

Isolated TAHO polypeptide-encoding nucleic acid can be used herein for recombinantly producing TAHO polypeptide using techniques well known in the art and as described herein. In turn, the produced TAHO polypeptides can be employed for generating anti-TAHO antibodies using techniques well known in the art and as described herein.

Antibodies specifically binding a TAHO polypeptide identified herein, as well as other molecules identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders, including cancer, in the form of pharmaceutical compositions.

If the TAHO polypeptide is intracellular and whole antibodies are used as inhibitors, internalizing antibodies are preferred. However, lipofections or liposomes can also be used to deliver the antibody, or an antibody fragment, into cells. Where antibody fragments are used, the smallest inhibitory fragment that specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an antibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology. See, e.g., Marasco et al., *Proc. Natl. Acad. Sci. USA*, 90: 7889-7893 (1993).

The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory

agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. Antibodies used in the examples are commercially available antibodies and include, but are not limited to, anti-CD180(eBioscience MRH73-11, BD Pharmingen G28-8) and Serotec MHR73), anti-CD20 (Ansell 2H7 and BD Pharmingen 2H7), anti-CD72 (BD Pharmingen J4-117), anti-CXCR5 (R&D Systems 51505), anti-CD22 (Ansell RFB4, DAKO To15, Diatec 157, Sigma HIB-22 and Monosan BL-BC34), anti-CD22 (Leinco RFB-4 and NeoMarkers 22C04), anti-CD21 (ATCC HB-135 and ATCC HB5), anti-HLA-DOB (BD Pharmingen DOB.L1), anti-CD79a (Caltag ZL7-4 and Serotec ZL7-4), anti-CD79b (Biomeda SN8 and BD Pharmingen CB-3), anti-CD19 (Biomeda CB-19), anti-FCER2 (Ansell BU38 and Serotec D3.6 and BD Pharmingen M-L233). The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, Va.

Example 1

Microarray Data Analysis of TAHO Expression

Microarray data involves the analysis of TAHO expression by the performance of DNA microarray analysis on a wide a variety of RNA samples from tissues and cultured cells. Samples include normal and cancerous human tissue and various kinds of purified immune cells both at rest and following external stimulation. These RNA samples may be analyzed according to regular microarray protocols on Agilent microarrays.

In this experiment, RNA was isolated from cells and cyanine-3 and cyanine-5 labeled cRNA probes were generated by in vitro transcription using the Agilent Low Input RNA Fluorescent Linear Amplification Kit (Agilent). Cyanine-5 was used to label the samples to be tested for expression of the PRO polypeptide, for example, the myeloma and plasma cells, and cyanine-3 was used to label the universal reference (the Stratagene cell line pool) with which the expression of the test samples were compared. 0.1 µg-0.2 mg of cyanine-3 and cyanine-5 labeled cRNA probe was hybridized to Agilent 60-mer oligonucleotide array chips using the In Situ Hybridization Kit Plus (Agilent). These probes were hybridized to microarrays. For multiple myeloma analysis, probes were hybridized to Agilent Whole Human Genome oligonucleotide microarrays using standard Agilent recommended conditions and buffers (Agilent).

The cRNA probes are hybridized to the microarrays at 60° C. for 17 hours on a hybridization rotator set at 4 RPM. After washing, the microarrays are scanned with the Agilent microarray scanner which is capable of exciting and detecting the fluorescence from the cyanine-3 and cyanine-5 fluorescent molecules (532 and 633 nm laser lines). The data for each gene on the 60-mer oligonucleotide array was extracted from the scanned microarray image using Agilent feature extrac-

tion software which accounts for feature recognition, background subtraction and normalization and the resulting data was loaded into the software package known as the Rosetta Resolver Gene Expression Data Analysis System (Rosetta Inpharmatics, Inc.). Rosetta Resolver includes a relational database and numerous analytical tools to store, retrieve and analyze large quantities of intensity or ratio gene expression data.

In this example, B cells and T cells (control) were obtained for microarray analysis. For isolation of naive and memory B cells and plasma cells, human peripheral blood mononuclear cells (PBMC) were separated from either leukopack provided by four healthy male donors or from whole blood of several normal donors. CD138+ plasma cells were isolated from PBMC using the MACS (Miltenyi Biotec) magnetic cell sorting system and anti-CD138 beads. Alternatively, total CD19+ B cells were selected with anti-CD19 beads and MACS sorting. After enrichment of CD19+ (purity around 90%), FACS (Moflo) sorting was performed to separate naive and memory B cells. Sorted cells were collected by subjecting the samples to centrifugation. The sorted cells were immediately lysed in LTR buffer and homogenized with QIAshredder (Qiagen) spin column and followed by RNeasy mini kit for RNA purification. RNA yield was variable from 0.4-10 µg and depended on the cell numbers.

As a control, T cells were isolated for microarray analysis. Peripheral blood CD8 cells were isolated from leukopacks by negative selection using the Stem Cell Technologies CD8 cell isolation kit (Rosette Separation) and further purified by the MACS magnetic cell sorting system using CD8 cell isolation kit and CD45RO microbeads were added to remove CD45RO cells (Miltenyi Biotec). CD8 T cells were divided into 3 samples with each sample subjected to the stimulation as follows: (1) anti-CD3 and anti-CD28, plus IL-12 and anti-IL4 antibody, (2) anti-CD3 and anti-CD29 without adding cytokines or neutralizing antibodies and (3) anti-CD3 and anti-CD28, plus IL-4, anti-IL12 antibody and anti-IFN-γ antibody. 48 hours after stimulation, RNA was collected. After 72 hours, cells were expanded by adding diluting 8-fold with fresh media. 7 days after the RNA was collected, CD8 cells were collected, washed and restimulated by anti-CD3 and anti-CD28. 16 hours later, a second collection of RNA was made. 48 hours after restimulation, a third collection of RNA was made. RNA was collected by using Qiagen Midi preps as per the instructions in the manual with the addition of an on-column DNase I digestion after the first RW1 wash step. RNA was eluted in RNase free water and subsequently concentrated by ethanol precipitation. Precipitated RNA was taken up in nuclease free water to a final minimum concentration of 0.5 µg/l.

Additional control microarrays were performed on RNA isolated from CD4+ T helper T cells, natural killer (NK) cells, neutrophils (N^{ph}il), CD14+, CD16+ and CD16- monocytes and dendritic cells (DC).

Additional microarrays were performed on RNA isolated from cancerous tissue, such as Non-Hodgkin's Lymphoma (NHL), follicular lymphoma (FL) and multiple myeloma (MM). Additional microarrays were performed on RNA isolated from normal cells, such as normal lymph node (NLN), normal B cells, such as B cells from centroblasts, centrocytes and follicular mantle, memory B cells, and normal plasma cells (PC), which are from the B cell lineage and are normal counterparts of the myeloma cell, such as tonsil plasma cells, bone marrow plasma cells (BM PC), CD19+ plasma cells (CD19+ PC), CD19- plasma cells (CD19- PC). Additional microarrays were performed on normal tissue, such as cerebellum, heart, prostate, adrenal, bladder, small intestine (s.

intestine), colon, fetal liver, uterus, kidney, placenta, lung, pancreas, muscle, brain, salivary, bone marrow (marrow), blood, thymus, tonsil, spleen, testes, and mammary gland.

The molecules listed below have been identified as being significantly expressed in B cells as compared to non-B cells. Specifically, the molecules are differentially expressed in naive B cells, memory B cells that are either IgG_A+ or IgM_A+ and plasma cells from either PBMC or bone marrow, in comparison to non-B-cells, for example T cells. Accordingly, these molecules represent excellent targets for therapy of tumors in mammals.

Molecule	specific expression in:	as compared to:
DNA105250 (TAHO1)	B cells	non-B cells
DNA150004 (TAHO2)	B cells	non-B cells
DNA182432 (TAHO3)	B cells	non-B cells
DNA225785 (TAHO4)	B cells	non-B cells
DNA225786 (TAHO5)	B cells	non-B cells
DNA225875 (TAHO6)	B cells	non-B cells
DNA226179 (TAHO7)	B cells	non-B cells
DNA226239 (TAHO8)	B cells	non-B cells
DNA226394 (TAHO9)	B cells	non-B cells
DNA226423 (TAHO10)	B cells	non-B cells
DNA227781 (TAHO11)	B cells	non-B cells
DNA227879 (TAHO12)	B cells	non-B cells
DNA256363 (TAHO13)	B cells	non-B cells
DNA332467 (TAHO14)	B cells	non-B cells
DNA58721 (TAHO15)	B cells	non-B cells
DNA335924 (TAHO16)	B cells	non-B cells
DNA340394 (TAHO17)	B cells	non-B cells
DNA56041 (TAHO18)	B cells	non-B cells
DNA59607 (TAHO19)	B cells	non-B cells
DNA257955 (TAHO20)	B cells	non-B cells
DNA329863 (TAHO21)	B cells	non-B cells
DNA346528 (TAHO22)	B cells	non-B cells
DNA212930 (TAHO23)	B cells	non-B cells
DNA335918 (TAHO24)	B cells	non-B cells
DNA225820 (TAHO25)	B cells	non-B cells
DNA88116 (TAHO26)	B cells	non-B cells
DNA227752 (TAHO27)	B cells	non-B cells
DNA119476 (TAHO28)	B cells	non-B cells
DNA254890 (TAHO29)	B cells	non-B cells
DNA219240 (TAHO30)	B cells	non-B cells
DNA37151 (TAHO31)	B cells	non-B cells
DNA210233 (TAHO32)	B cells	non-B cells
DNA35918 (TAHO33)	B cells	non-B cells
DNA260038 (TAHO34)	B cells	non-B cells
DNA334818 (TAHO35)	B cells	non-B cells
DNA257501 (TAHO36)	B cells	non-B cells

Summary

In FIGS. 73-101, significant mRNA expression was generally indicated as a ratio value of greater than 2 (vertical axis of FIGS. 73-101). In FIGS. 73-101, any apparent expression in non-B cells, such as in prostate, spleen, etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(1) TAHO1 (also referred herein as LY64 and CD180) was significantly expressed in non-hodgkin's lymphoma (NHL) and normal B (NB) cell samples (FIG. 73).

(2) TAHO2 (also referred herein as MS4A1 and CD20) was significantly expressed in non-hodgkin's lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN) and normal B (NB) cells. Further, TAHO2 was significantly expressed in normal tonsil and spleen (FIG. 74).

(3) TAHO3 (also referred herein as SPAP1 and FcRH2) was significantly expressed in non-hodgkin's lymphoma (NHL) and follicular lymphoma (FL) and memory B cells (mem B). Further TAHO3 was significantly expressed in blood and spleen (FIG. 75). However, as indicated above, any apparent expression in non-B cells, such as in prostate,

spleen, blood etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(4) TAHO4 (also referred herein as CD79a) was significantly expressed in non-hodgkin's lymphoma (NHL) multiple myeloma (MM) samples and normal cerebellum and normal blood. Further TAHO4 was significantly expressed in cerebellum, blood and spleen (FIG. 76). However, as indicated above, any apparent expression in non-B cells, such as in prostate, spleen, blood etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(5) TAHO5 (also referred herein as CD79b) was significantly expressed in non-hodgkin's lymphoma (NHL) (FIG. 77).

(6) TAHO6 (also referred herein as CR2 and CD21) was significantly expressed in non-hodgkin's lymphoma (NHL) and normal lymph node (NLN). Further TAHO6 was significantly expressed in spleen (FIG. 78).

(7) TAHO8 (also referred herein as CD72) was significantly expressed in non-hodgkin's lymphoma (NHL), multiple myeloma (MM) and follicular lymphoma (FL) and normal tonsil (FIG. 79). However, as indicated above, any apparent expression in non-B cells, such as in prostate, spleen, blood, tonsil etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(8) TAHO9 (also referred herein as P2RX5) was significantly expressed in normal B cells (circulating and lymph-node derived B cells) and not significantly expressed in non B cells. Further, TAHO9 was significantly expressed in normal plasma cells and in multiple myeloma (FIGS. 80A-80B). In normal tissues, expression of TAHO9 is relatively low, but with significant expression in lymphoid organs such as spleen and thymus. FIGS. 80A-80B are shown as two panels. The panel in FIG. 80A represents normal tissue from left to right as follows: salivary gland (1), bone marrow (2), tonsil (3), fetal liver (4), blood (5), bladder (6), thymus (7), spleen (8), adrenal gland (9), fetal brain (10), small intestine (11), testes (12), heart (13), colon (14), lung (15), prostate (16), brain cerebellum (17), skeletal muscle (18), kidney (19), pancreas (20), placenta (21), uterus (22) and mammary gland (23). The panel in FIG. 80B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(9) TAHO10 (also referred herein as HLA-DOB) was significantly expressed in multiple myeloma (MM), non-hodgkin's lymphoma (NHL) (FIG. 81).

(10) TAHO11 (also referred herein as CXCR5 and BLR1) was significantly expressed in non-hodgkin's lymphoma (NHL), follicular lymphoma (FL), normal lymph node (NLN), normal B cells (NB), centroblasts and follicular mantle cells, and normal spleen and normal tonsil (FIG. 82). However, as indicated above, any apparent expression in non-B cells, such as in prostate, spleen, blood, tonsil, etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(11) TAHO12 (also referred herein as FCER2) was significantly expressed in normal B cells (NB), multiple myeloma (MM) and prostate (FIG. 83). However, as indicated above, any apparent expression in non-B cells, such as in prostate, spleen, blood, tonsil, etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(12) TAHO13 (also referred herein as GPR2) was significantly expressed in multiple myeloma (MM), and normal blood (FIGS. 84A-84B). FIGS. 84A-84B are shown as two panels. The panel in FIG. 84A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 84B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(13) TAHO15 (also referred herein as LRRC4 and NAG14) was significantly expressed in non-hodgkin's lymphoma (NHL) (FIG. 85). As shown in FIG. 72, PRO1111 (TAHO15) was significantly expressed and upregulated in bone marrow plasma cells and multiple myeloma as compared to low expression in non-B cells, including neutrophils, T cells and natural killer (NK) cells. PRO1111 is also significantly expressed in some non-hodgkin lymphoma cells.

(14) TAHO17 (also referred herein as FcRH1) was significantly expressed in normal B cells (NB), and memory B cells (FIG. 86).

(15) TAHO18 (also referred herein as IRTA2) was significantly expressed in non-hodgkin's lymphoma (NHL) (FIG. 87).

(16) TAHO20 (also referred herein as FcRH3) was significantly expressed in normal B cells (NB) and multiple myeloma (MM). Further, TAHO20 was detected in expressed in colon, placenta, lung and spleen (FIG. 88). However, as indicated above, any apparent expression in non-B cells, such as in prostate, spleen, blood, tonsil, etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(17) TAHO21 (also referred herein as IRTA1) was significantly expressed in non-hodgkin's lymphoma (NHL), centrocytes and memory B cells (FIG. 89).

(18) TAHO25 (also referred herein as CD19) was significantly expressed in non-hodgkin's lymphoma (NHL), normal lymph node (NLN), follicular lymphoma (FL), centroblasts, centrocytes, memory B cells and follicular mantle cells. Further TAHO25 was significantly expressed in tonsil and spleen (FIG. 90). However, as indicated above, any apparent expression in non-B cells, such as in prostate, spleen, blood, tonsil, etc. may represent an artifact, infiltration of normal tissue by lymphocytes or loss of sample integrity by the vendor.

(19) TAHO26 (also referred herein as CD22) was significantly expressed in normal B cells (NB) (FIG. 91).

(20) TAHO27 (also referred herein as CXCR3) was significantly expressed in multiple myeloma cells (FIG. 92A-92B). FIGS. 92A-92B are shown as two panels. The panel in FIG. 92A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 92B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(21) TAHO28 (also referred herein as SILV1) was significantly expressed in normal plasma cells, and more significantly expressed on multiple myeloma cells (FIGS. 93A-93B). FIGS. 93A-93B are shown as two panels. The panel in FIG. 93A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (1), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 93B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(22) TAHO29 (also referred herein as KCNK4) was significantly expressed in normal plasma cells and in multiple myeloma cells (FIGS. 94A-94B). In normal tissues, expression of TAHO29 is significantly expressed in normal testes. FIGS. 94A-94B are shown as two panels. The panel in FIG. 94A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (1), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 94B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone mar-

row cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(23) TAHO30 (also referred herein as CXorf1) was significantly expressed on multiple myeloma cells (FIGS. 95A-95B). In normal tissues, expression of TAHO30 is significantly expressed in normal testes. FIGS. 95A-95B are shown as two panels. The panel in FIG. 95A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 95B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(24) TAHO31 (also referred herein as LRRN5) was significantly expressed in normal plasma cells, and more significantly expressed on multiple myeloma cells (FIGS. 96A-96B). In normal tissues, expression of TAHO31 is significantly expressed in cerebellum. FIGS. 96A-96B are shown as two panels. The panel in FIG. 96A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 96B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(25) TAHO32 (also referred herein as UNQ9308) was significantly expressed in normal plasma cells, and more significantly expressed on multiple myeloma cells (FIGS. 97A-97B). TAHO32 was also significantly expressed in normal prostate. FIGS. 97A-97B are shown as two panels. The panel in FIG. 97A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 97B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), mono-

cytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(26) TAHO33 (also referred herein as IGSF4B) was significantly expressed in multiple myeloma cells (FIGS. 98A-98D). FIGS. 98A-98B are shown as two panels. The panel in FIG. 98A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 98B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(27) TAHO34 (also referred herein as UNQ13267) was significantly expressed in normal plasma cells, and more significantly expressed on multiple myeloma cells (FIGS. 99A-99D). TAHO34 was also significantly expressed in normal blood. FIGS. 99A-99B are shown as two panels. The panel in FIG. 99A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 99B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(28) TAHO35 (also referred herein as FLJ12681) was significantly expressed in normal plasma cells, and more significantly expressed on multiple myeloma cells (FIGS. 100A-100B). FIGS. 100A-100B are shown as two panels. The panel in FIG. 100A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (11), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 100B represents the samples tested from left to

right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

(29) TAHO36 (also referred herein as UNQ12376) was significantly expressed in normal plasma cells, and more significantly expressed on multiple myeloma cells (FIGS. 101A-101B). FIGS. 101A-101B are shown as two panels. The panel in FIG. 101A represents normal tissue from left to right as follows: brain cerebellum (1), pancreas (2), fetal liver (3), placenta (4), adrenal gland (5), kidney (6), small intestine (7), colon (8), prostate (9), lung (10), uterus (1), bladder (12), bone marrow (13), tonsil (14), spleen (15), thymus (16), blood (17), fetal brain (18), salivary gland (19), testes (20), heart (21), skeletal muscle (22) and mammary gland (23). The panel in FIG. 101B represents the samples tested from left to right as follows: NK cells (1), neutrophils (2), CD4+ cells (3), CD8+ cells (4), CD34+ cells (5), normal B cells (6), monocytes (7), dendritic cells (8), multiple myeloma cells (9-11), memory B cells (12), naive B cells (13), centrocytes (14), centroblasts (15-16), centrocytes (17), memory B cells (18), naive B cells (19), normal B cells (20-38), multiple myeloma cells (39), CD138+ cells (40), multiple myeloma cells (41-46), tonsil plasma cells (47), bone marrow plasma cells (48), multiple myeloma cells (49-60), centrocytes (61), plasma bone marrow cells (62-70), plasma cell CD19+ (71), plasma cell CD19- (72), multiple myeloma cells (73-75).

As TAHO1-36 have been identified as being significantly expressed in B cells and in samples from B-cell associated diseases, such as Non-Hodgkin's lymphoma, follicular lymphoma and multiple myeloma as compared to non-B cells as detected by microarray analysis, the molecules are excellent targets for therapy of tumors in mammals, including B-cell associated cancers, such as lymphomas, leukemias, myelomas and other cancers of hematopoietic cells.

Example 2

Quantitative Analysis of TAHO mRNA Expression

In this assay, a 5' nuclease assay (for example, TaqMan®) and real-time quantitative PCR (for example, Mx3000P™ Real-Time PCR System (Stratagene, La Jolla, Calif.)), were used to find genes that are significantly overexpressed in a specific tissue type, such as B cells, as compared to a different cell type, such as other primary white blood cell types, and which further may be overexpressed in cancerous cells of the specific tissue type as compared to non-cancerous cells of the specific tissue type. The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor gene expression in real time. Two oligonucleotide primers (whose sequences are based upon the gene or EST sequence of interest) are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when

the two dyes are located close together as they are on the probe. During the PCR amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the Mx3000™ Real-Time PCR System. The system consists of a thermocycler, a quartz-tungsten lamp, a photomultiplier tube (PMT) for detection and a computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the PMT. The system includes software for running the instrument and for analyzing the data. The starting material for the screen was mRNA (50 ng/well run in duplicate) isolated from a variety of different white blood cell types (Neutrophil (Neutr), Natural Killer cells (NK), Dendritic cells (Dend.), Monocytes (Mono), T cells (CD4+ and CD8+ subsets), stem cells (CD34+) as well as 20 separate B cell donors (donor Ids 310, 330, 357, 362, 597, 635, 816, 1012, 1013, 1020, 1072, 1074, 1075, 1076, 1077, 1086, 1096, 1098, 1109, 1112) to test for donor variability. All RNA was purchased commercially (AllCells, LLC, Berkeley, Calif.) and the concentration of each was measured precisely upon receipt. The mRNA is quantitated precisely, e.g., fluorometrically.

5' nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The Δ Ct values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample. As one Ct unit corresponds to 1 PCR cycle or approximately a 2-fold relative increase relative to normal, two units corresponds to a 4-fold relative increase, 3 units corresponds to an 8-fold relative increase and so on, one can quantitatively measure the relative fold increase in mRNA expression between two or more different tissues. The lower the Ct value in a sample, the higher the starting copy number of that particular gene. If a standard curve is included in the assay, the relative amount of each target can be extrapolated and facilitates viewing of the data as higher copy numbers also have relative quantities (as opposed to higher copy numbers have lower Ct values) and also corrects for any variation of the generalized 1 Ct equals a 2 fold increase rule. Using this technique, the molecules listed below have been identified as being significantly over-expressed (i.e., at least 2 fold) in a single (or limited number) of specific tissue or cell types as compared to a different tissue or cell type (from both the same and different tissue donors) with some also being identified as being significantly over-expressed (i.e., at least 2 fold) in cancerous cells when compared to normal cells of the particular tissue or cell type, and thus, represent excellent polypeptide targets for therapy of cancer in mammals.

Molecule	specific expression in:	as compared to:
DNA105250 (TAHO1)	B cells	non-B cells
DNA150004 (TAHO2)	B cells	non-B cells
DNA182432 (TAHO3)	B cells	non-B cells
DNA225785 (TAHO4)	B cells	non-B cells
DNA225786 (TAHO5)	B cells/CD34+ cells	non-B cells

-continued

Molecule	specific expression in:	as compared to:
DNA225875 (TAHO6)	B cells	non-B cells
DNA226239 (TAHO8)	B cells	non-B cells
DNA226394 (TAHO9)	B cells	non-B cells
DNA226423 (TAHO10)	B cells	non-B cells
DNA227781 (TAHO11)	B cells	non-B cells
DNA227879 (TAHO12)	B cells	non-B cells
DNA2260953 (TAHO13)	B cells	non-B cells
DNA335924 (TAHO16)	B cells	non-B cells
DNA340394 (TAHO17)	B cells	non-B cells
DNA225820 (TAHO25)	B cells	non-B cells
DNA88116 (TAHO26)	B cells	non-B cells

15 Summary

TAHO1-TAHO6, TAHO8-TAHO13, TAHO16-TAHO17 and TAHO25-TAHO26 expression levels in total RNA isolated from purified B cells or from B cells from 20 B cell donors (310-1112) (AllCells) and averaged (Avg. B) was significantly higher than respective TAHO1-TAHO6, TAHO8-TAHO13, TAHO16-17 and TAHO25-TAHO26 expression levels in total RNA isolated from several white blood cell types, neutrophils (Neutr), natural killer cells (NK) (a T cell subset), dendritic cells (Dend), monocytes (Mono), CD4+ T cells, CD8+ T cells, CD34+ stem cells (data not shown).

Accordingly, as TAHO1-TAHO6, TAHO8-TAHO13, TAHO16-TAHO17 and TAHO25-TAHO26 are significantly expressed on B cells as compared to non-B cells as detected by TaqMan analysis, the molecules are excellent targets for therapy of tumors in mammals, including B-cell associated cancers, such as lymphomas (i.e. Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

Example 3

In Situ Hybridization

In situ hybridization is a powerful and versatile technique for the detection and localization of nucleic acid sequences within cell or tissue preparations. It may be useful, for example, to identify sites of gene expression, analyze the tissue distribution of transcription, identify and localize viral infection, follow changes in specific mRNA synthesis and aid in chromosome mapping.

In situ hybridization was performed following an optimized version of the protocol by Lu and Gillett, *Cell Vision* 1:169-176 (1994), using PCR-generated ³³P-labeled riboprobes. Briefly, formalin-fixed, paraffin-embedded human tissues were sectioned, deparaffinized, deproteinized in proteinase K (20 g/ml) for 15 minutes at 37° C., and further processed for in situ hybridization as described by Lu and Gillett, supra. A [³³-P] UTP-labeled antisense riboprobe was generated from a PCR product and hybridized at 55° C. overnight. The slides were dipped in Kodak NTB2 nuclear track emulsion and exposed for 4 weeks.

³³P-Riboprobe Synthesis

6.0 μ l (125 mCi) of ³³P-UTP (Amersham BF 1002, SA<2000 Ci/mmol) were speed vac dried. To each tube containing dried ³³P-UTP, the following ingredients were added:

2.0 μ l 5 \times transcription buffer

1.0 μ l DTT (100 mM)

2.0 μ l NTP mix (2.5 mM:10 μ ; each of 10 mM GTP, CTP & ATP+10 μ l H₂O)

- 1.0 μ l UTP (50 μ M)
- 1.0 μ l Rnasin
- 1.0 μ l DNA template (1 μ g)
- 1.0 μ l H₂O
- 1.0 μ l RNA polymerase (for PCR products T3=AS, T7=S, usually)

The tubes were incubated at 37° C. for one hour. 1.0 μ l RQ1 DNase were added, followed by incubation at 37° C. for 15 minutes. 90 μ l TE (10 mM Tris pH 7.6/1 mM EDTA pH 8.0) were added, and the mixture was pipetted onto DE81 paper. The remaining solution was loaded in a Microcon-50 ultra-filtration unit, and spun using program 10 (6 minutes). The filtration unit was inverted over a second tube and spun using program 2 (3 minutes). After the final recovery spin, 100 μ l TE were added. 1 μ l of the final product was pipetted on DE81 paper and counted in 6 ml of Biofluor II.

The probe was run on a TBE/urea gel. 1-3 μ l of the probe or 5 μ l of RNA Mrk III were added to 3 μ l of loading buffer. After heating on a 95° C. heat block for three minutes, the probe was immediately placed on ice. The wells of gel were flushed, the sample loaded, and run at 180-250 volts for 45 minutes. The gel was wrapped in saran wrap and exposed to XAR film with an intensifying screen in -70° C. freezer one hour to overnight.

³³P-Hybridization

A. Pretreatment of Frozen Sections

The slides were removed from the freezer, placed on aluminium trays and thawed at room temperature for 5 minutes. The trays were placed in 55° C. incubator for five minutes to reduce condensation. The slides were fixed for 10 minutes in 4% paraformaldehyde on ice in the fume hood, and washed in 0.5 \times SSC for 5 minutes, at room temperature (25 ml 20 \times SSC+975 ml SQ H₂O). After deproteination in 0.5 μ g/ml proteinase K for 10 minutes at 37° C. (12.5 μ l of 10 mg/ml stock in 250 ml prewarmed RNase-free RNase buffer), the sections were washed in 0.5 \times SSC for 10 minutes at room temperature. The sections were dehydrated in 70%, 95%, 100% ethanol, 2 minutes each.

B. Pretreatment of Paraffin-Embedded Sections

The slides were deparaffinized, placed in SQ H₂O, and rinsed twice in 2 \times SSC at room temperature, for minutes each time. The sections were deproteinated in 20 μ g/ml proteinase K (500 μ l of 10 mg/ml in 250 ml RNase-free RNase buffer; 37° C., 15 minutes)—human embryo, or 8 \times proteinase K (100 μ l in 250 ml RNase buffer, 37° C., 30 minutes)—formalin tissues. Subsequent rinsing in 0.5 \times SSC and dehydration were performed as described above.

C. Prehybridization

The slides were laid out in a plastic box lined with Box buffer (4 \times SSC, 50% formamide)—saturated filter paper.

D. Hybridization

1.0 \times 10⁶ cpm probe and 1.0 μ l tRNA (50 mg/ml stock) per slide were heated at 95° C. for 3 minutes. The slides were cooled on ice, and 48 μ l hybridization buffer were added per slide. After vortexing, 50 μ l ³³P mix were added to 50 μ l prehybridization on slide. The slides were incubated overnight at 55° C.

E. Washes

Washing was done 2 \times 10 minutes with 2 \times SSC, EDTA at room temperature (400 ml 20 \times SSC+16 ml 0.25M EDTA, V_r=4 L), followed by RNaseA treatment at 37° C. for 30 minutes (500 μ l of 10 mg/ml in 250 ml RNase buffer=20 μ g/ml). The slides were washed 2 \times 10 minutes with 2 \times SSC, EDTA at room temperature. The stringency wash conditions were as follows: 2 hours at 55° C., 0.1 \times SSC, EDTA (20 ml 20 \times SSC+16 ml EDTA, V_r=4 L).

F. Oligonucleotides

In situ analysis was performed on a variety of DNA sequences disclosed herein. The oligonucleotides employed for these analyses were obtained so as to be complementary to the nucleic acids (or the complements thereof) as shown in the accompanying figures.

- (1) DNA225785 (TAHO4)
- 10 p1 5'-GGGCACCAAGAACC GAATCAT- (SEQ ID NO: 72)
3'
- p2 5'-CCTAGAGGCAGCGATT AAGGG- (SEQ ID NO: 73)
3'
- (2) DNA257955 (TAHO20)
- 15 p1 5'-TCAGCACGTGGATTCGAGTCA- (SEQ ID NO: 74)
3'
- p2 5'-GTGAGGACGGGGCGAGAC-3' (SEQ ID NO: 75)

G. Results

In situ analysis was performed on a variety of DNA sequences disclosed herein. The results from these analyses are as follows.

(1) DNA225785 (TAHO4)

Expression was observed in lymphoid cells. Specifically, in normal tissues, expression was observed in spleen and lymph nodes and coincides with B cell areas, such as germinal centers, mantle, and marginal zones. Significant expression was also observed in tissue sections of a variety of malignant lymphomas, including Hodgkin's lymphoma, follicular lymphoma, diffuse large cell lymphoma, small lymphocytic lymphoma and non-Hodgkin's lymphoma. This data is consistent with the potential role of this molecule in hematopoietic tumors, specifically B-cell tumors.

(2) DNA257955 (TAHO20)

Expression was observed in benign and neoplastic lymphoid cells. Specifically, in normal tissues, expression was observed in B cell areas, such as germinal centers, mantle and marginal zones, and in white pulp tissue of the spleen. This data is consistent with the potential role of this molecule in hematopoietic tumors, specifically B-cell tumors.

Example 4

Use of TAHO as a Hybridization Probe

The following method describes use of a nucleotide sequence encoding TAHO as a hybridization probe for, i.e., detection of the presence of TAHO in a mammal.

DNA comprising the coding sequence of full-length or mature TAHO as disclosed herein can also be employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of TAHO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled TAHO-derived probe to the filters is performed in a solution of 50% formamide, 5 \times SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2 \times Denhardt's solution, and 10% dextran sulfate at 42° C. for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1 \times SSC and 0.1% SDS at 42° C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence TAHO can then be identified using standard techniques known in the art.

Expression of TAHO in *E. coli*

This example illustrates preparation of an unglycosylated form of TAHO by recombinant expression in *E. coli*.

The DNA sequence encoding TAHO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., *Gene*, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the TAHO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized TAHO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

TAHO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding TAHO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) Ion galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30° C. with shaking until an O.D. 600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate.2H₂O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30° C. with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1 M and 0.02 M, respectively, and the solution is stirred overnight at 4° C. This

step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4° C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4° C. for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded TAHO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Certain of the TAHO polypeptides disclosed herein have been successfully expressed and purified using this technique(s).

Example 6

Expression of TAHO in Mammalian Cells

This example illustrates preparation of a potentially glycosylated form of TAHO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published Mar. 15, 1989), is employed as the expression vector. Optionally, the TAHO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the TAHO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-TAHO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM

supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μg pRK5-TAHO DNA is mixed with about 1 μg DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500 μl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl_2 . To this mixture is added, dropwise, 500 μl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO_4 , and a precipitate is allowed to form for 10 minutes at 25° C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37° C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 $\mu\text{Ci/ml}$ ^{35}S -cysteine and 200 $\mu\text{Ci/ml}$ ^{35}S -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of TAHO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, TAHO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompariyac et al., *Proc. Natl. Acad. Sci.*, 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μg pRK5-TAHO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 $\mu\text{g/ml}$ bovine insulin and 0.1 $\mu\text{g/ml}$ bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed TAHO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, TAHO can be expressed in CHO cells. The pRK5-TAHO can be transfected into CHO cells using known reagents such as CaPO_4 or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ^{35}S -methionine. After determining the presence of TAHO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed TAHO can then be concentrated and purified by any selected method.

Epitope-tagged TAHO may also be expressed in host CHO cells. The TAHO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged TAHO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged TAHO can then be concentrated and purified by any selected method, such as by Ni^{2+} -chelate affinity chromatography.

TAHO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., *Current Protocols of Molecular Biology*, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., *Nucl. Acids Res.* 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Qiagen), Dosper® or Fugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3×10^7 cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mL of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μm filtered PS20 with 5% 0.2 μm diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37° C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3×10^5 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Pat. No. 5,122,469, issued Jun. 16, 1992 may actually be used. A 3 L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33° C., and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μm filter. The filtrate was either stored at 4° C. or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 mL Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4° C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly

purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C .

Immuno-adhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μL of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Certain of the TAHO polypeptides disclosed herein have been successfully expressed and purified using this technique(s).

Example 7

Expression of TAHO in Yeast

The following method describes recombinant expression of TAHO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of TAHO from the ADH2/GAPDH promoter. DNA encoding TAHO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of TAHO. For secretion, DNA encoding TAHO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native TAHO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of TAHO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant TAHO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing TAHO may further be purified using selected column chromatography resins.

Certain of the TAHO polypeptides disclosed herein have been successfully expressed and purified using this technique(s).

Example 8

Expression of TAHO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of TAHO in Baculovirus-infected insect cells.

The sequence coding for TAHO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids-such as pVL1393 (Novagen). Briefly, the

sequence encoding TAHO or the desired portion of the coding sequence of TAHO such as the sequence encoding an extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmin-gen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4-5 days of incubation at 28°C ., the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., *Baculovirus expression vectors: A Laboratory Manual*, Oxford: Oxford University Press (1994).

Expressed poly-his tagged TAHO can then be purified, for example, by Ni^{2+} -chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., *Nature*, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl_2 ; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni^{2+} -NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A_{280} with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni^{2+} -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged TAHO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) TAHO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Certain of the TAHO polypeptides disclosed herein have been successfully expressed and purified using this technique(s).

Example 9

Preparation of Antibodies that Bind TAHO

This example illustrates preparation of monoclonal antibodies which can specifically bind TAHO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, supra. Immunogens that may be employed include purified TAHO, fusion proteins containing TAHO, and cells expressing recombinant TAHO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the TAHO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, Mont.) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-TAHO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of immunogen. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against immunogen. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against immunogen is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-immunogen monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

Antibodies directed against certain of the TAHO polypeptides disclosed herein can be successfully produced using this technique(s). More specifically, functional monoclonal antibodies that are capable of recognizing and binding to TAHO protein (as measured by standard ELISA, FACS sorting analysis and/or immunohistochemistry analysis) can be successfully generated against the following TAHO proteins as disclosed herein: TAHO1 (DNA105250), TAHO2 (DNA150004), TAHO3 (DNA182432), TAHO4 (DNA225785), TAHO5 (DNA225786), TAHO6 (DNA225875), TAHO7 (DNA226179), TAHO8 (DNA226239), TAHO9 (DNA226239), TAHO10 (DNA226423), TAHO11 (DNA227781), TAHO12 (DNA227879), TAHO13 (DNA256363), TAHO14 (DNA332467), TAHO15 (DNA58721), TAHO16 (DNA335924), TAHO17 (DNA340394), TAHO18 (DNA56041), TAHO19 (DNA59607), TAHO20 (DNA257955), TAHO21 (DNA329863), TAHO22 (DNA346528), TAHO23 (DNA212930) and TAHO24 (DNA225820), TAHO 25 (DNA225820), TAHO26 (DNA88116), and TAHO27 (DNA227752), TAHO28 (DNA119476), TAHO29 (DNA254890), TAHO30 (DNA219240), TAHO31 (DNA37151), TAHO32 (DNA210233), TAHO33 (DNA35918), TAHO34 (DNA260038), TAHO35 (DNA334818) and TAHO36 (DNA257501).

In addition to the preparation of monoclonal antibodies directed against the TAHO polypeptides as described herein, many of the monoclonal antibodies can be successfully con-

jugated to a cell toxin for use in directing the cellular toxin to a cell (or tissue) that expresses a TAHO polypeptide of interest (both in vitro and in vivo). For example, toxin (e.g., DM1) derivitized monoclonal antibodies can be successfully generated to the following TAHO polypeptides as described herein: TAHO1 (DNA105250), TAHO2 (DNA150004), TAHO3 (DNA182432), TAHO4 (DNA225785), TAHO5 (DNA225786), TAHO6 (DNA225875), TAHO7 (DNA226179), TAHO8 (DNA226239), TAHO9 (DNA226239), TAHO10 (DNA226423), TAHO11 (DNA227781), TAHO12 (DNA227879), TAHO13 (DNA256363), TAHO14 (DNA332467), TAHO15 (DNA58721), TAHO16 (DNA335924), TAHO17 (DNA340394), TAHO18 (DNA56041), TAHO19 (DNA59607), TAHO20 (DNA257955), TAHO21 (DNA329863), TAHO22 (DNA346528), TAHO23 (DNA212930) and TAHO24 (DNA335918), TAHO 25 (DNA225820), TAHO26 (DNA88116), TAHO27 (DNA227752), TAHO28 (DNA119476), TAHO29 (DNA254890), TAHO30 (DNA219240), TAHO31 (DNA37151), TAHO32 (DNA210233), TAHO33 (DNA35918), TAHO34 (DNA260038), TAHO35 (DNA334818) and TAHO36 (DNA257501).

Example 10

Purification of TAHO Polypeptides Using Specific Antibodies

Native or recombinant TAHO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-TAHO polypeptide, mature TAHO polypeptide, or pre-TAHO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the TAHO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-TAHO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of TAHO polypeptide by preparing a fraction from cells containing TAHO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble TAHO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble TAHO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of TAHO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/TAHO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3,

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or a high concentration of a chaotrope such as urea or thiocyanate ion), and TAHO polypeptide is collected.

Example 11

In Vitro Tumor Cell Killing Assay

Mammalian cells expressing the TAHO polypeptide of interest may be obtained using standard expression vector and cloning techniques. Alternatively, many tumor cell lines expressing TAHO polypeptides of interest are publicly available, for example, through the ATCC and can be routinely identified using standard ELISA or FACS analysis. Anti-TAHO polypeptide monoclonal antibodies (commercially available and toxin conjugated derivatives thereof) may then be employed in assays to determine the ability of the antibody to kill TAHO polypeptide expressing cells in vitro.

For example, cells expressing the TAHO polypeptide of interest are obtained as described above and plated into 96 well dishes. In one analysis, the antibody/toxin conjugate (or naked antibody) is included throughout the cell incubation for a period of 4 days. In a second independent analysis, the cells are incubated for 1 hour with the antibody/toxin conjugate (or naked antibody) and then washed and incubated in the absence of antibody/toxin conjugate for a period of 4 days. Cell viability is then measured using the CellTiter-Glo Luminescent Cell Viability Assay from Promega (Cat#G7571). Untreated cells serve as a negative control.

B cell lines (ARH-77, BJAB, Daudi, DOHH-2, Su-DHL-4, Raji and Ramos) were prepared at 5000 cells/well in separate sterile round bottom 96 well tissue culture treated plates (Cellstar 650 185). Cells were assay media (RPMI 1460, 1% L-Glutamine, 10% fetal bovine serum (FBS; from Hyclone) and 10 mM HEPES). Cells were immediately placed in a 37° C. incubator overnight. Antibody drug conjugates (using commercially available anti-CD19, anti-CD20, anti-CD21, anti-CD79A, anti-CD79B) were diluted at 2x10 µg/ml in assay medium. Conjugates were linked with crosslinkers SMCC or disulfide linker SPP to DM1 toxin. Further, conjugates may be linked with Vc-PAB to MMAE toxin. Herceptin based conjugates (SMCC-DM1 or SPP-DM1) were used as negative controls. Free L-DM1 equivalent to the conjugate loading dose was used as a positive control. Samples were vortexed to ensure homogenous mixture prior to dilution. The antibody drug conjugates were further diluted serially 1:3. The cell lines were loaded 50 µl of each sample per row using a Rapidplate® 96/384 Zymark automation system. When the entire plate was loaded, the plates were reincubated for 3 days to permit the toxins to take effect. The reactions were stopped by applying 10 µl/well of Cell Glo (Promega, Cat. #G7571/2/3) to all the wells for 10 minutes. The 100 µl of the stopped well were transferred into 96 well white tissue culture treated plates, clear bottom (Costar 3610) and the luminescence was read and reported as relative light units (RLU). TAHO antibodies for this experiment included commercially available antibodies, including anti-TAHO4/CD79a (Caltag ZL7-4), anti-TAHO5/CD79b (Biomedica SN8), anti-TAHO6/CD21 (ATCC HB5), anti-TAHO26/CD22 (Leinco RFB-4) and anti-TAHO25/CD19 (Biomedica CB-19).

Summary

(1) Anti-TAHO26/CD22 antibody conjugated to DM1 toxin (CD22-SPP-DM1 and CD22-SMCC-DM1) showed significant tumor cell killing when compared to anti-TAHO26/CD22 antibody alone or negative control anti-HER2 conjugated to DM1 toxin (anti-HER2-SMCC-DM1)

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in RAJI or RAMOS cells. Further, greater tumor cell killing was observed with CD22-SPP-DM1 compared to CD22-SMCC-DM1.

(2) Anti-TAHO25/CD19 antibody conjugated to DM1 toxin (CD19-SPP-DM1 and CD19-SMCC-DM1) showed significant tumor cell killing when compared to anti-TAHO25/CD19 antibody alone or negative control anti-HER2 conjugated to DM1 toxin (anti-HER2-SMCC-DM1) in RAJI or RAMOS cells. Further, greater tumor cell killing was observed with CD19-SMCC-DM1 compared to CD19-SPP-DM1.

(3) Anti-TAHO6/CD21 antibody conjugated to DM1 toxin (CD21-SPP-DM1 and CD2-SMCC-DM1) showed weak tumor cell killing when compared to anti-TAHO6/CD21 antibody alone or negative control anti-HER2 conjugated to DM1 toxin (anti-HER2-SMCC-DM1) in RAJI or RAMOS cells. Further, greater tumor cell killing was observed with CD21-SPP-DM1 compared to CD21-SMCC-DM1.

(4) Anti-TAHO4/CD79A antibody conjugated to DM1 toxin (CD79A-SMCC-DM1) showed significant tumor cell killing when compared to anti-TAHO4/CD79A antibody alone or negative control anti-HER2 conjugated to DM1 toxin (anti-HER2-SMCC-DM1) in RAMOS cells.

(5) Anti-TAHO5/CD79B antibody conjugated to DM1 toxin (CD79BSMCC-DM1) showed significant tumor cell killing when compared to anti-TAHO5/CD79B antibody alone or negative control anti-HER2 conjugated to DM1 toxin (anti-HER2-SMCC-DM1) in RAJI or RAMOS cells.

Anti-TAHO polypeptide monoclonal antibodies are useful for reducing in vitro tumor growth of tumors, including B-cell associated cancers, such as lymphomas (i.e. Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

Example 12

In Vivo Tumor Cell Killing Assay

To test the efficacy of conjugated or unconjugated anti-TAHO polypeptide monoclonal antibodies, the effect of anti-TAHO antibody on tumors in mice were analyzed. Female CB17 ICR SCID mice (6-8 weeks of age from Charles Rivers Laboratories; Hollister, Calif.) were inoculated subcutaneously with 5x10⁶ RAJI cells or 2x10⁷ BJAB-luciferase cells. Tumor volume was calculated based on two dimensions, measured using calipers, and was expressed in mm³ according to the formula: V=0.5axb², where a and b are the long and the short diameters of the tumor, respectively. Data collected from each experimental group were expressed as mean±SE. Mice were separated into groups of 8-10 mice with a mean tumor volume between 100-200 mm³, at which point intravenous (i.v.) treatment began at the antibody dose of 5 mg/kg weekly for two to three weeks. Tumors were measured either once or twice a week throughout the experiment. Mice were euthanized before tumor volumes reached 3000 mm³ or when tumors showed signs of impending ulceration. All animal protocols were approved by an Institutional Animal Care and Use Committee (IACUC). Linkers between the antibody and the toxin that were used were SPP, SMCC or cys-MC-vc-PAB (a valine-citrulline (vc) dipeptide linker reagent having a maleimide component and a para-aminobenzylcarbamoyl (PAB) self-immolative component. Toxins used were DM1 or MMAE. TAHO antibodies for this experiment included commercially available antibodies, including anti-TAHO4/CD79a (Caltag ZL7-4), anti-TAHO5/CD79b (Biomedica

SN8), anti-TAHO6/CD21 (ATCC HB135) and anti-TAHO25/CD19 (Biomedica CB-19).

Summary

(1) Anti-TAHO6/CD21 antibody conjugated with DM1 toxin (anti-CD21-SPP-DM1) showed inhibition of tumor growth in SCID mice with RAJI tumors when treated weekly with 5 mg/kg of antibody compared to anti-CD21 antibodies and herceptin antibodies conjugated to DM1 toxin (anti-Herceptin-SMCC-DM1 and anti-Herceptin-SPP-DM1). Specifically, at day 19, 8 out of 8 mice treated with anti-CD21-SPP-DM1 showed complete regression of tumors. At day 19, 8 out of 8 mice treated with anti-CD21, anti-herceptin-SPP-DM1, anti-herceptin-SMCC-DM1 or anti-CD21-SMCC-DM1 showed tumor incidence. At day 19, 7 out of 8 mice treated with anti-CD20-SMCC-DM1 antibody showed tumor incidence.

(2) Anti-TAHO6/CD21 antibody conjugated with MMAE toxin (anti-CD21-cys-Mc-vc-PAB-MMAE) showed inhibition of tumor growth in SCID mice with RAJI tumors when treated with 5 mg/kg of antibody compared to negative control anti-CD1 antibody or anti-herceptin antibody. Specifically at day 14, 5 out of 9 mice treated with anti-CD21-cys-MC-vc-PAB-MMAE showed partial regression of tumors and 4 out of 9 mice treated with anti-CD21-cys-MC-vc-PAB-MMAE showed complete regression of tumors. At day 14, 10 out of 10 mice treated with anti-herceptin or anti-CD21 antibody showed tumor incidence.

(3) Anti-TAHO25/CD19 antibody conjugated with DM1 toxin (anti-CD19-SPP-DM1) showed inhibition of tumor growth in SCID mice with RAJI tumors when treated with 5 mg/kg of antibody compared to negative control anti-CD19 antibody conjugated to DM1 (anti-CD19-SMCC-DM1), anti-CD22 antibody conjugated to DM1 (anti-CD22-SMCC-DM1) and anti-herceptin antibody conjugated to DM1 (anti-herceptin-smcc-DM1 or anti-herceptin-spp-DM1). Specifically at day 14, 2 out of 6 mice treated with anti-CD19-SPP-DM1 showed partial regression of tumors and 3 out of 6 mice treated with anti-CD19-SPP-DM1 showed complete regression of tumors. At day 14, 8 out of 8 mice treated with anti-herceptin-SPP-DM1, anti-herceptin-SMCC-DM1, anti-CD19-SMCC-DM1 or anti-CD22-SMCC-DM1 showed tumor incidence.

(4) Anti-TAHO4/CD79A antibody conjugated with DM1 (anti-CD79A-SMCC-DM1) showed inhibition of tumor growth in SCID mice with RAMOS tumors compared to negative control, anti-herceptin-SMCC-DM1.

(5) Anti-TAHO5/CD79B antibody conjugated with DM1 (anti-CD79B-SMCC-DM1) showed inhibition of tumor growth in SCID mice with RAMOS tumors compared to negative control, anti-herceptin-SMCC-DMA. Anti-TAHO5/CD79B antibody conjugated with DM1 (anti-CD79B-SMCC-DM1) showed inhibition of tumor growth in SCID mice with BJAB-luciferase tumors compared to negative control, anti-herceptin-SMCC-DM1 or anti-herceptin antibody. The level of inhibition by anti-CD79B-SMCC-DM1 antibodies was similar to the level of inhibition by anti-CD20 antibodies. Specifically at day 15, 1 out of 10 mice treated with anti-CD79B-SMCC-DM1 showed partial regression of tumors and 9 out of 10 mice treated with anti-CD79B-SMCC-DM1 showed complete regression of tumors. At day 15, 10 out of 10 mice treated with anti-herceptin-SMCC-DM1, anti-herceptin antibody showed tumor incidence. At day 15, 5 out of 10 mice treated with anti-CD20 antibodies showed partial regression of tumors.

Anti-TAHO polypeptide monoclonal antibodies are useful for reducing in vivo tumor growth of tumors in mammals, including B-cell associated cancers, such as lymphomas (i.e.

Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

Example 13

Immunohistochemistry

To determine tissue expression of TAHO polypeptide and to confirm the microarray results from Example 1, immunohistochemical detection of TAHO polypeptide expression was examined in snap-frozen and formalin-fixed paraffin-embedded (FFPE) lymphoid tissues, including palatine tonsil, spleen, lymph node and Peyer's patches from the Genentech Human Tissue Bank.

Prevalence of TAHO target expression was evaluated on FFPE lymphoma tissue microarrays (Cybrdi) and a panel of 24 frozen human lymphoma specimens. Frozen tissue specimens were sectioned at 5 μ m, air-dried and fixed in acetone for 5 minutes prior to immunostaining. Paraffin-embedded tissues were sectioned at 5 μ m and mounted on SuperFrost Plus microscope slides (VWR).

For frozen sections, slides were placed in TBST, 1% BSA and 10% normal horse serum containing 0.05% sodium azide for 30 minutes, then incubated with Avidin/Biotin blocking kit (Vector) reagents before addition of primary antibody. Mouse monoclonal primary antibodies (commercially available) were detected with biotinylated horse anti-mouse IgG (Vector), followed by incubation in Avidin-Biotin peroxidase complex (ABC Elite, Vector) and metal-enhanced diaminobenzidine tetrahydrochloride (DAB, Pierce). Control sections were incubated with isotype-matched irrelevant mouse monoclonal antibody (Pharmingen) at equivalent concentration. Following application of the ABC-HRP reagent, sections were incubated with biotinyl-tyramide (Perkin Elmer) in amplification diluent for 5-10 minutes, washed, and again incubated with ABC-HRP reagent. Detection was using DAB as described above.

FFPE human tissue sections were dewaxed into distilled water, treated with Target Retrieval solution (Dako) in a boiling water bath for 20 minutes, followed by a 20 minute cooling period. Residual endogenous peroxidase activity was blocked using 1 \times Blocking Solution (KPL) for 4 minutes. Sections were incubated with Avidin/Biotin blocking reagents and Blocking Buffer containing 10% normal horse serum before addition of the monoclonal antibodies, diluted to 0.5-5.0 μ g/ml in Blocking Buffer. Sections were then incubated sequentially with biotinylated anti-mouse secondary antibody, followed by ABC-HRP and chromogenic detection with DAB. Tyramide Signal Amplification, described above, was used to increase sensitivity of staining for a number of TAHO targets (CD21, CD22, HLA-DOB).

Summary

(1) TAHO26 (CD22) showed strong labeling of mantle zone B cells and weaker, but significant labeling of germinal centers as detected with primary antibody clone RFB-4 (Leinco) in frozen human tonsil tissue and clone 22C04 (Neomarkers) in FFPE human tonsil tissue (data not shown).

(2) TAHO10 (HLA-DOB) showed punctuate labeling pattern, possibly due to labeling of TAHO10 on intracellular vesicles as detected with clone DOB.L1 (BD/Pharmingen) in FFPE human tonsil tissue (data not shown).

(3) TAHO8 (CD72) showed punctuate labeling pattern, possibly due to labeling of TAHO8 on intracellular vesicles as detected with clone J4-117 (BD/Pharmingen) in frozen human tonsil tissue (data not shown).

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(4) TAHO1 (CD180) showed punctuate labeling pattern, possibly due to labeling of TAHO1 on intracellular vesicles as detected with clone MHR73 (Serotec) in frozen human tonsil tissue (data not shown).

(5) TAHO6 (CD21) showed strong labeling of follicular dendritic cells in germinal centers and mature B cells within mantle zone as detected with clone HB-135 (ATCC) in FFPE human tonsil tissue and using tyramide signal amplification (TSA) (data not shown).

(6) TAHO11(CXCR5) showed significant labeling in both mantle zone and germinal centers as detected with clone 51505 (R&D Systems) and using a Cy3-conjugated anti-mouse antibody (R&D Systems) in frozen human tonsil.

Accordingly, in light of TAHO1, TAHO6, TAHO8, TAHO10, TAHO11 and TAHO26 expression pattern as assessed by immunohistochemistry in tonsil samples, a lymphoid organ where B cells develop, the molecules are excellent targets for therapy of tumors in mammals, including B-cell associated cancers, such as lymphomas (i.e. Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

Example 14

Flow Cytometry

To determine the expression of TAHO molecules, FACS analysis was performed using a variety of cells, including normal cells and diseased cells, such as chronic lymphocytic leukemia (CLL) cells.

A. Normal Cells: TAHO2 (CD20), TAHO1 (CD180), TAHO26 (CD22), TAHO4 (CD79A), TAHO5 (CD79B), TAHO8 (CD72), TAHO11 (CXCR5)

For tonsil B cell subtypes, the fresh tonsil was minced in cold HBSS and passed through a 70 um cell strainer. Cells were washed once and counted. CD19+ B cells were enriched using the AutoMACS (Miltenyi). Briefly, tonsil cells were blocked with human IgG, incubated with anti-CD19 microbeads, and washed prior to positive selection over the AutoMACS. A fraction of CD19+ B cells were saved for flow cytometric analysis of plasma cells. Remaining CD19+ cells were stained with FITC-CD77, PE-IgD, and APC-CD38 for sorting of B-cell subpopulations. CD19+ enrichment was analyzed using PE-Cy5-CD19, and purity ranged from 94-98% CD19+. Tonsil B subpopulations were sorted on the MoFlo by Michael Hamilton at flow rate 18,000-20,000 cells/second. Follicular mantle cells were collected as the IgD+/CD38- fraction, memory B cells were IgD-/CD38-, centrocytes were IgD-/CD38+/CD77-, and centroblasts were IgD-/CD38+/CD77+. Cells were either stored in 50% serum overnight, or stained and fixed with 2% paraformaldehyde. For plasma cell analysis, total tonsil B cells were stained with CD138-PE, CD20-FITC, and biotinylated antibody to the target of interest detected with streptavidin-PE-Cy5. Tonsil B subpopulations were stained with biotinylated antibody to the target of interest, detected with streptavidin-PE-Cy5. Flow analysis was done on the BD FACSCaliber, and data was further analyzed using FlowJo software v 4.5.2 (TreeStar). Biotin-conjugated antibodies which were commercially available such as TAHO2/CD20 (2H7 from Ancell), TAHO1/CD180 (MHR73-11 from eBioscience), TAHO8/CD72 (JF-117 from BD Pharmingen), TAHO26/CD22 (RFB4 from Ancell), TAHO11/CXCR5 (51505 from R&D Systems), TAHO4/CD79A (ZL7-4 from Serotec) and TAHO5/CD79B (CB-3 from BD Pharmingen) were used in the flow cytometry.

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Summary of TAHO2 (CD20), TAHO1 (CD180), TAHO26 (CD22), TAHO4 (CD79A), TAHO5 (CD79B), TAHO8 (CD72), TAHO11 (CXCR5) on Normal Cells

The expression pattern on sorted tonsil-B subtypes was performed using monoclonal antibody specific to the TAHO polypeptide of interest. TAHO2 (CD20) (using anti-CD20, 2H7 from BD Pharmingen), TAHO26 (CD22) (using anti-CD22, RFB4 from Ancell), TAHO4 (CD79A) (using anti-CD79A), TAHO5 (CD79B) (using anti-CD79B), TAHO8 (CD72) (using anti-CD72), TAHO1 (CD180) (using anti-CD180, MHR73-11 from eBioscience) and TAHO11 (using anti-CXCR5, 51505 from R&D Systems) showed significant expression in memory B cells, follicular mantle cells, centroblasts and centrocytes (data not shown).

The expression pattern on tonsil plasma cells was performed using monoclonal antibody specific to the TAHO polypeptide of interest. TAHO26 (CD22) (using anti-CD22, RFB4 from Ancell), TAHO4 (CD79A) (using anti-CD79A), TAHO5 (CD79B) (using anti-CD79B), TAHO1 (CD180) (using anti-CD180, MHR73-11 from eBioscience) and TAHO8 (CD72) (using anti-CD72) showed significant expression in plasma cells (data not shown).

Accordingly, in light of TAHO2, TAHO11, TAHO26, TAHO04, TAHO5, TAHO8 and TAHO11 expression pattern on tonsil-B subtypes as assessed by FACS, the molecules are excellent targets for therapy of tumors in mammals, including B-cell associated cancers, such as lymphomas (i.e. Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

B. CLL Cells: TAHO11 (CXCR5), TAHO4 (CD79A), TAHO5 (CD79B), TAHO26 (CD22), TAHO12 (CD23/FCER2), TAHO1 (CD180)

The following purified or fluorochrome-conjugated mAbs were used for flow cytometry of CLL samples: CD5-PE, CD19-PerCP Cy5.5, CD20-FITC, CD20-APC (commercially available from BD Pharmingen). Further, commercially available biotinylated antibodies against CD22 (RFB4 from Ancell), CD23 (M-L233 from BD Pharmingen), CD79A (ZL7-4 from Serotec), CD79B (CB-3 from BD Pharmingen), CD180 (MHR73-11 from eBioscience), CXCR5 (51505 from R&D Systems) were used for the flow cytometry. The CD5, CD19 and CD20 antibodies were used to gate on CLL cells and P1 staining was performed to check the cell viability.

Cells (10^6 cells in 100 ml volume) were first incubated with 1 mg of each CD5, CD19 and CD20 antibodies and 10 mg each of human and mouse gamma globulin (Jackson ImmunoResearch Laboratories, West Grove, Pa.) to block the non-specific binding, then incubated with optimal concentrations of mAbs for 30 minutes in the dark at 4° C. When biotinylated antibodies were used, streptavidin-PE or streptavidin-APC (Jackson ImmunoResearch Laboratories) were then added according to manufacture's instructions. Flow cytometry was performed on a FACS calibur (BD Biosciences, San Jose, Calif.). Forward scatter (FSC) and side scatter (SSC) signals were recorded in linear mode, fluorescence signals in logarithmic mode. Dead cells and debris were gated out using scatter properties of the cells. Data were analysed using CellQuest Pro software (BD Biosciences) and FlowJo (Tree Star Inc.).

Summary of TAHO11 (CXCR5), TAHO4 (CD79A), TAHO5 (CD79B), TAHO26 (CD22), TAHO12 (CD23/FCER2), TAHO1 (CD180) on CLL Samples

The expression pattern on CLL samples was performed using monoclonal antibody specific to the TAHO polypeptide of interest. TAHO11 (CXCR5), TAHO4 (CD79A), TAHO5

(CD79B), TAHO26 (CD22), TAHO12 (CD23/FCER2), TAHO1 (CD180) showed significant expression in CLL samples (data not shown).

Accordingly, in light of TAHO11, TAHO4, TAHO5, TAHO26, TAHO12 and TAHO1 expression pattern on chronic lymphocytic leukemia (CLL) samples as assessed by FACS, the molecules are excellent targets for therapy of tumors in mammals, including B-cell associated cancers, such as lymphomas (i.e. Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

Example 15

TAHO Internalization

Internalization of the TAHO antibodies into B-cell lines was assessed in Raji, Ramos, Daudi and other B cell lines, including ARH77, SuDHL4, U698M, huB and BJAB cell lines.

One ready-to-split 15 cm dish of B-cells ($\sim 5 \times 10^6$ cells) with cells for use in up to 20 reactions was used. The cells were below passage 25 (less than 8 weeks old) and growing healthily without any mycoplasma.

In a loosely-capped 15 ml Falcon tube add 1 $\mu\text{g/ml}$ mouse anti-TAHO antibody to 2.5×10^6 cells in 2 ml normal growth medium (e.g. RPMI/10% FBS/1% glutamine) containing 1:10 FcR block (MACS kit, dialyzed to remove azide), 1% pen/strep, 5 μM pepstatin A, 10 $\mu\text{g/ml}$ leupeptin (lysosomal protease inhibitors) and 25 $\mu\text{g/ml}$ Alexa488-transferrin (which labeled the recycling pathway and indicated which cells were alive; alternatively Ax488 dextran fluid phase marker may be used to mark all pathways) for 24 hours in a 37° C. 5% CO₂ incubator. For quickly-internalizing antibodies, time-points every 5 minutes were taken. For time-points taken less than 1 hour, 1 ml complete carbonate-free medium (Gibco 18045-088+10% FBS, 1% glutamine, 1% pen/strep, 10 mM Hepes pH 7.4) was used and the reactions were performed in a 37° C. waterbath instead of the CO₂ incubator.

After completion of the time course, the cells were collected by centrifugation (1500 rpm 4° C. for 5 minutes in G6-SR or 2500 rpm 3 minutes in 4° C. benchtop eppendorf centrifuge), washed once in 1.5 ml carbonate free medium (in Eppendorfs) or 10 ml medium for 15 ml Falcon tubes. The cells were subjected to a second centrifugation and resuspended in 0.5 ml 3% paraformaldehyde (EMS) in PBS for 20 minutes at room temp to allow fixation of the cells.

All following steps are followed by a collection of the cells via centrifugation. Cells were washed in PBS and then quenched for 10 minutes in 0.5 ml 50 mM NH₄Cl (Sigma) in PBS and permeabilized with 0.5 ml 0.1% Triton-X-100 in PBS for 4 minutes during a 4 minute centrifugation spin. Cells were washed in PBS and subjected to centrifugation. 1 $\mu\text{g/ml}$ Cy3-anti mouse (or anti-species 1° antibody was) added to detect uptake of the antibody in 200 μl complete carbonate free medium for 20 minutes at room temperature.

Cells were washed twice in carbonate free medium and resuspend in 25 μl carbonate free medium and the cells were allowed to settle as a drop onto one well of a polylysine-coated 8-well LabtekII slide for at least one hour (or overnight in fridge). Any non-bound cells were aspirated and the slides were mounted with one drop per well of DAPI-containing Vectashield under a 50x24 mm coverslip. The cells were examined under 100x objective for internalization of the antibodies.

Summary

(1) TAHO25/CD19 (as detected using anti-CD19 antibody Biomedica CB-19) was internalized within 20 minutes in Ramos and Daudi cells, arriving in lysosomes by 1 hour. In Raji and ARH77 cells, TAHO25/CD19 internalization was not detectable in 20 hours.

(2) Significant TAHO6/CR2 (as detected using anti-CR2 antibody ATCC HB-135) internalization was not detectable in Raji cells and in Daudi cells in 20 hours.

(3) TAHO26/CD22 (as detected using anti-CD22 antibody Leinco RFB4) was internalized in 5 minutes in Raji cells, in 5 minutes in Ramos cells, in 5 minutes in Daudi cells, and in 5 minutes in ARH77 cells and was delivered to lysosomes by 1 hour. TAHO26/CD22 (as detected using anti-CD22 antibodies, DAKO To15, Diatec 157, Sigma HIB-22 or Monosan BL-BC34) was internalized in 5 minutes in Raji cells and was delivered to lysosomes by 1 hour.

(4) Significant TAHO12/FCER2 (as detected using anti-FCER2 antibody Ancell BU38 or Serotec D3.6) internalization was not detectable in ARH77 cells in 20 hours.

(5) Significant TAHO8/CD72 (as detected using anti-CD72 antibody BD Pharmingen J4-117) internalization was not detectable in 20 hours in SuDHL4 cells.

(6) TAHO4/CD79a (as detected using anti-CD79a antibody Serotec ZL7-4) was internalized in 1 hour in Ramos cells, in 1 hour in Daudi cells and in 1 hour in SuDHL4 cells, and was delivered to lysosomes in 3 hours.

(7) TAHO1/CD180 (as detected using anti-CD180 antibody BD Pharmingen G28-8) was internalized in minutes in SuDHL4 cells and was delivered to lysosomes in 20 hours.

(8) Significant TAHO11/CXCR5 (as detected using anti-CXCR5 antibody R&D Systems 51505) internalization was not detectable in 20 hours in U698M cells.

(9) TAHO5/CD79b (as detected using anti-CD79b antibody Ancell SN8) internalizes in 20 minutes in Ramos, Daudi and Su-DHL4 cells and is delivered to the lysosomes in 1 hour.

Accordingly, in light of TAHO25, TAHO26, TAHO4, TAHO1 and TAHO5 internalization on B-cell lines as assessed by immunofluorescence using respective anti-TAHO antibodies, the molecules are excellent targets for therapy of tumors in mammals, including B-cell associated cancers, such as lymphomas (i.e. Non-Hodgkin's Lymphoma), leukemias (i.e. chronic lymphocytic leukemia), myelomas (i.e. multiple myeloma) and other cancers of hematopoietic cells.

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 ttatcatgag gatgtcacc ttgggaacag ctcggcccc tctggaggag 1100
 gggcctcctt caacctctct ttgactgcag aacattctgg aaactactcc 1150
 tgtgaggcca acaacggcct gggggcccag tgcagtgagg cagtgccagt 1200
 ctccatctca ggacctgatg gctatagaag agacctcatg acagctggag 1250
 ttctctgggg actgtttggt gtccttggtt tcaactggtg tgetttgctg 1300
 ttgtatgcct tgtccacaa gatatcagga gaaagttctg cactaatga 1350
 acccagaggg gcttcaggc caaatcctca agagttcacc tattcaagcc 1400
 caacccaga catggaggag ctgcagccag tgtatgcaa tgtggctct 1450

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gtagatgtgg atgtggttta ttctcaggtc tggagcatgc agcagccaga      1500
aagctcagca aacatcagga cacttctgga gaacaaggac toccaagtca      1550
tctactcttc tgtgaagaaa tcataacact tggaggaatc agaaggggaag    1600
atcaacagca aggatggggc atcattaaga cttgctataa aaccttatga      1650
aatgcttga ggcttatcac ctgccacagc cagaacgtgc ctcaggaggc      1700
acctcctgtc atttttgtcc tgatgatggt tcttctccaa tatcttcttt    1750
tacctatcaa tattcattga actgctgcta catccagaca ctgtgcaaat     1800
aaattatttc tgctaccttc aaaaaaaaaa aaaaaaaaaa atgcag         1846

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<210> SEQ ID NO 6

<211> LENGTH: 508

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

```

Met Leu Leu Trp Ser Leu Leu Val Ile Phe Asp Ala Val Thr Glu
 1                               5 10 15
Gln Ala Asp Ser Leu Thr Leu Val Ala Pro Ser Ser Val Phe Glu
                20 25 30
Gly Asp Ser Ile Val Leu Lys Cys Gln Gly Glu Gln Asn Trp Lys
                35 40 45
Ile Gln Lys Met Ala Tyr His Lys Asp Asn Lys Glu Leu Ser Val
                50 55 60
Phe Lys Lys Phe Ser Asp Phe Leu Ile Gln Ser Ala Val Leu Ser
                65 70 75
Asp Ser Gly Asn Tyr Phe Cys Ser Thr Lys Gly Gln Leu Phe Leu
                80 85 90
Trp Asp Lys Thr Ser Asn Ile Val Lys Ile Lys Val Gln Glu Leu
                95 100 105
Phe Gln Arg Pro Val Leu Thr Ala Ser Ser Phe Gln Pro Ile Glu
                110 115 120
Gly Gly Pro Val Ser Leu Lys Cys Glu Thr Arg Leu Ser Pro Gln
                125 130 135
Arg Leu Asp Val Gln Leu Gln Phe Cys Phe Phe Arg Glu Asn Gln
                140 145 150
Val Leu Gly Ser Gly Trp Ser Ser Ser Pro Glu Leu Gln Ile Ser
                155 160 165
Ala Val Trp Ser Glu Asp Thr Gly Ser Tyr Trp Cys Lys Ala Glu
                170 175 180
Thr Val Thr His Arg Ile Arg Lys Gln Ser Leu Gln Ser Gln Ile
                185 190 195
His Val Gln Arg Ile Pro Ile Ser Asn Val Ser Leu Glu Ile Arg
                200 205 210
Ala Pro Gly Gly Gln Val Thr Glu Gly Gln Lys Leu Ile Leu Leu
                215 220 225
Cys Ser Val Ala Gly Gly Thr Gly Asn Val Thr Phe Ser Trp Tyr
                230 235 240
Arg Glu Ala Thr Gly Thr Ser Met Gly Lys Lys Thr Gln Arg Ser
                245 250 255
Leu Ser Ala Glu Leu Glu Ile Pro Ala Val Lys Glu Ser Asp Ala
                260 265 270
Gly Lys Tyr Tyr Cys Arg Ala Asp Asn Gly His Val Pro Ile Gln

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275	280	285
Ser Lys Val Val Asn Ile Pro Val Arg Ile Pro Val Ser Arg Pro		
290	295	300
Val Leu Thr Leu Arg Ser Pro Gly Ala Gln Ala Ala Val Gly Asp		
305	310	315
Leu Leu Glu Leu His Cys Glu Ala Leu Arg Gly Ser Pro Pro Ile		
320	325	330
Leu Tyr Gln Phe Tyr His Glu Asp Val Thr Leu Gly Asn Ser Ser		
335	340	345
Ala Pro Ser Gly Gly Gly Ala Ser Phe Asn Leu Ser Leu Thr Ala		
350	355	360
Glu His Ser Gly Asn Tyr Ser Cys Glu Ala Asn Asn Gly Leu Gly		
365	370	375
Ala Gln Cys Ser Glu Ala Val Pro Val Ser Ile Ser Gly Pro Asp		
380	385	390
Gly Tyr Arg Arg Asp Leu Met Thr Ala Gly Val Leu Trp Gly Leu		
395	400	405
Phe Gly Val Leu Gly Phe Thr Gly Val Ala Leu Leu Leu Tyr Ala		
410	415	420
Leu Phe His Lys Ile Ser Gly Glu Ser Ser Ala Thr Asn Glu Pro		
425	430	435
Arg Gly Ala Ser Arg Pro Asn Pro Gln Glu Phe Thr Tyr Ser Ser		
440	445	450
Pro Thr Pro Asp Met Glu Glu Leu Gln Pro Val Tyr Val Asn Val		
455	460	465
Gly Ser Val Asp Val Asp Val Val Tyr Ser Gln Val Trp Ser Met		
470	475	480
Gln Gln Pro Glu Ser Ser Ala Asn Ile Arg Thr Leu Leu Glu Asn		
485	490	495
Lys Asp Ser Gln Val Ile Tyr Ser Ser Val Lys Lys Ser		
500	505	

<210> SEQ ID NO 7
 <211> LENGTH: 1107
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 7

tgctgcaact caaactaacc aaccactgg gagaagatgc ctgggggtcc	50
aggagtcctc caagctctgc ctgccacat cttcctcctc ttctgtgt	100
ctgctgteta cctgggcct gggtgccagg cctgtggat gcacaaggtc	150
ccagcatcat tgatggtgag cctgggggaa gacgcccact tccaatgcc	200
gcacaatagc agcaacaacg ccaacgtcac ctggtggcgc gtcctccatg	250
gcaactacac gtggcccct gagttcttgg gcccgggcga ggacccaat	300
ggtacgctga tcatccagaa tgtgaacaag agccatgggg gcatatacgt	350
gtgccgggtc caggaggga acgagtcata ccagcagtc tgccgcaact	400
acctccgct gcgcccagcg cccccaggc cttcctgga catgggggag	450
ggcaccaaga accgaatcat cacagccgag gggatcatcc tcctgttctg	500
cgcggtggtg cctgggacgc tgctgctgtt caggaaacga tggcagaacg	550
agaagctcgg gttggatgcc ggggatgaat atgaagatga aaacctttat	600

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gaaggcctga acctggacga ctgctccatg tatgaggaca tctcccgggg      650
cctccagggc acctaccagg atgtgggcag cctcaacata ggagatgtcc      700
agctggagaa gccgtgacac cctactcct gccaggctgc ccccgctgc      750
tgtgcacca gctccagtgt ctcagctcac ttccctggga cattctcctt      800
tcagcccttc tgggggcttc cttagtccata ttccccagc ggggggtggg      850
agggtaacct cactcttctc cagggcagc ctccttgac tccctgggg      900
gtgtcccact cttcttccct ctaaactgcc ccacctccta acctaatccc      950
cacgccccgc tgcctttccc aggctcccct caccagcgg gtaatgagcc     1000
cttaategct gcctctaggg gagctgattg tagcagctc gttagtgtca     1050
ccccctctc cctgatctgt cagggccact tagtgataat aaattcttcc     1100
caactgc                                                    1107

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<210> SEQ ID NO 8

<211> LENGTH: 226

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

```

Met Pro Gly Gly Pro Gly Val Leu Gln Ala Leu Pro Ala Thr Ile
 1                    5          10          15
Phe Leu Leu Phe Leu Leu Ser Ala Val Tyr Leu Gly Pro Gly Cys
 20          25          30
Gln Ala Leu Trp Met His Lys Val Pro Ala Ser Leu Met Val Ser
 35          40          45
Leu Gly Glu Asp Ala His Phe Gln Cys Pro His Asn Ser Ser Asn
 50          55          60
Asn Ala Asn Val Thr Trp Trp Arg Val Leu His Gly Asn Tyr Thr
 65          70          75
Trp Pro Pro Glu Phe Leu Gly Pro Gly Glu Asp Pro Asn Gly Thr
 80          85          90
Leu Ile Ile Gln Asn Val Asn Lys Ser His Gly Gly Ile Tyr Val
 95          100          105
Cys Arg Val Gln Glu Gly Asn Glu Ser Tyr Gln Gln Ser Cys Gly
 110          115          120
Thr Tyr Leu Arg Val Arg Gln Pro Pro Pro Arg Pro Phe Leu Asp
 125          130          135
Met Gly Glu Gly Thr Lys Asn Arg Ile Ile Thr Ala Glu Gly Ile
 140          145          150
Ile Leu Leu Phe Cys Ala Val Val Pro Gly Thr Leu Leu Leu Phe
 155          160          165
Arg Lys Arg Trp Gln Asn Glu Lys Leu Gly Leu Asp Ala Gly Asp
 170          175          180
Glu Tyr Glu Asp Glu Asn Leu Tyr Glu Gly Leu Asn Leu Asp Asp
 185          190          195
Cys Ser Met Tyr Glu Asp Ile Ser Arg Gly Leu Gln Gly Thr Tyr
 200          205          210
Gln Asp Val Gly Ser Leu Asn Ile Gly Asp Val Gln Leu Glu Lys
 215          220          225
Pro

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<210> SEQ ID NO 9

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<211> LENGTH: 1270

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

```

caggggacag gctgcagccg gtgcagttac acgttttctt ccaaggagcc      50
tcggacgttg tcacgggttt ggggtcgggg acagagcagt gaccatggcc      100
aggctggcgt tgtctcctgt gccacgccac tggatgggtg cgttgctgct      150
gctgctctca gctgagccag taccagcagc cagatcggag gaccgggtacc     200
ggaatcccaa aggtagtgtc tgttcgcgga tctggcagag cccacgtttc     250
atagccagga aacggggcct cacggtgaaa atgcactgct acatgaacag     300
cgctccggc aatgtgagct ggctctggaa gcaggagatg gacgagaatc     350
cccagcagct gaagctggaa aagggccgca tggaaagatc ccagaacgaa     400
tctctcgcca cctcaccat ccaaggcacc cggtttgagg acaatggcat     450
ctacttctgt cagcagaagt gcaacaacac ctccggagtc taccagggct     500
gcggcacaga gctgcgagtc atgggattca gcaccttggc acagctgaag     550
cagaggaaca cgctgaagga tggatcacc atgatccaga cgctgctgat     600
catcctcttc atcatcgtgc ctatcttct gctgctggac aaggatgaca     650
gcaaggctgg catggaggaa gatcacacct acgagggcct ggacattgac     700
cagacagcca cctatgagga catagtgcg ctgcggacag gggaaagtga     750
gtggtctgta ggtgagcacc cagggcagga gtgagagcca ggtcgcccca     800
tgacctgggt gcaggctccc tggcctcagt gactgcttcg gagctgacctg     850
gctcatggcc caaccctttt cctggacccc ccagctggcc tctgaagctg     900
gcccaccaga gctgccatth gtctccagcc cctgggtccc agctcttgcc     950
aaagggctcg gtagtagagg acaacagggc agcaacttgg agggagtctt    1000
ctggggatgg acgggaccca gccttctggg ggtgctatga ggtgatccgt    1050
ccccacacat gggatggggg aggcagagac tggccagag cccgcaaatg    1100
gactcggagc cgagggcctc ccagcagagc ttgggaaggg ccatggaccc    1150
aactgggccc cagaagagcc acaggaacat cattctcttc ccgcaaccac    1200
tcccacccca gggaggccct ggctccagc gccttcccc gtggaataaa    1250
cggtgtgtcc tgagaaacca    1270

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<210> SEQ ID NO 10

<211> LENGTH: 229

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 10

```

Met Ala Arg Leu Ala Leu Ser Pro Val Pro Ser His Trp Met Val
 1             5             10             15
Ala Leu Leu Leu Leu Leu Ser Ala Glu Pro Val Pro Ala Ala Arg
 20             25             30
Ser Glu Asp Arg Tyr Arg Asn Pro Lys Gly Ser Ala Cys Ser Arg
 35             40             45
Ile Trp Gln Ser Pro Arg Phe Ile Ala Arg Lys Arg Gly Phe Thr
 50             55             60
Val Lys Met His Cys Tyr Met Asn Ser Ala Ser Gly Asn Val Ser

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	65		70		75
Trp Leu Trp Lys	Gln Glu Met Asp Glu Asn Pro Gln Gln Leu Lys				
	80		85		90
Leu Glu Lys Gly Arg Met Glu Glu Ser Gln Asn Glu Ser Leu Ala					
	95		100		105
Thr Leu Thr Ile Gln Gly Ile Arg Phe Glu Asp Asn Gly Ile Tyr					
	110		115		120
Phe Cys Gln Gln Lys Cys Asn Asn Thr Ser Glu Val Tyr Gln Gly					
	125		130		135
Cys Gly Thr Glu Leu Arg Val Met Gly Phe Ser Thr Leu Ala Gln					
	140		145		150
Leu Lys Gln Arg Asn Thr Leu Lys Asp Gly Ile Ile Met Ile Gln					
	155		160		165
Thr Leu Leu Ile Ile Leu Phe Ile Ile Val Pro Ile Phe Leu Leu					
	170		175		180
Leu Asp Lys Asp Asp Ser Lys Ala Gly Met Glu Glu Asp His Thr					
	185		190		195
Tyr Glu Gly Leu Asp Ile Asp Gln Thr Ala Thr Tyr Glu Asp Ile					
	200		205		210
Val Thr Leu Arg Thr Gly Glu Val Lys Trp Ser Val Gly Glu His					
	215		220		225
Pro Gly Gln Glu					

<210> SEQ ID NO 11

<211> LENGTH: 3934

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 11

```

gccctcccag agctgccgga cgctcgoggg tctcggaacg catcccgccg      50
eggggggttc ggccgtggca tgggcccgc gggcctgctc ggggttttct      100
tggtctctgt cgcaccgggg gtccctggga tttcttgttg ctctctccg      150
cctatcctaa atggccggat tagttattat tctaccccc ttgctgttgg      200
taccgtgata aggtacagtt gttcaggtag ctctccgctc attggagaaa      250
aaagtctatt atgcataact aaagacaaa tggtggaac ctgggataaa      300
cctgctccta aatgtgaata tttcaataaa tattcttctt gccctgagcc      350
catagtacca ggaggatata aaattagagg ctctaccccc tacagacatg      400
gtgattctgt gacatttgcc tgtaaaacca acttctccat gaacggaaac      450
aagtctgttt ggtgtcaagc aaataatat tgggggcccga caccgactacc      500
aacctgtgta agtgttttcc ctctcgagtg tccagcactt cctatgatcc      550
acaatggaca tcacacaagt gagaatgttg gctccattgc tccaggattg      600
tctgtgactt acagctgtga atctggttac ttgcttgttg gagaaaagat      650
cattaactgt ttgtcttcgg gaaaatggag tgctgtcccc cccacatgtg      700
aagaggcacg ctgtaaatct ctaggacgat ttccaatgg gaaggtaaag      750
gagcctccaa ttctccgggt tgggtgtaact gcaaactttt tctgtgatga      800
agggatcgca ctgcaaggcc cacctctag tgggtgtgta attgctggac      850
agggagtgtc ttggacccaa atgccagtat gtgaagaaat tttttgccc      900
tcacctcccc ctattctcaa tggaagacat ataggcaact cactagcaaa      950

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tgtctcatat ggaagcatag tcaacttacac ttgtgaccog gaaccagagg	1000
aaggagtgaa cttcatcctt attggagaga gcaactctccg ttgtacagtt	1050
gatagtcaga agactgggac ctggagtggc cctgccccac gctgtgaact	1100
ttctacttct gcggttcagt gtccacatcc ccagatccta agaggccgaa	1150
tggtatctgg gcagaaagat cgatatacct ataacgacac tgtgatattt	1200
gcttgcatgt ttggcttcac cttgaagggc agcaagcaaa tccgatgcaa	1250
tgccaaggc acatgggagc catctgcacc agtctgtgaa aaggaatgcc	1300
aggccccctc taacatcctc aatgggcaaa aggaagatag acacatggtc	1350
cgctttgacc ctggaacatc tataaaatat agctgtaacc ctggctatgt	1400
gctggtggga gaagaatcca tacagtgtac ctctgagggg gtgtggacac	1450
cccctgtacc ccaatgcaaa gtggcagcgt gtgaagctac aggaaggcaa	1500
ctcttgacaa aaccccagca ccaatttgtt agaccagatg tcaactcttc	1550
ttgtggtgaa gggtaacaagt taagtgggag tgtttatcag gagtgtcaag	1600
gcacaattcc ttggtttatg gagattcgtc tttgtaaaga aatcacctgc	1650
ccaccacccc ctgttatcta caatggggca cacaccggga gttccttaga	1700
agattttcca tatggaacca cggtcactta cacatgtaac cctgggcccag	1750
aaagaggagt ggaattcagc ctcatggag agagcaccat ccgttgtaca	1800
agcaatgatc aagaaaggag cacctggagt ggccctgctc ccctatgtaa	1850
actttccctc cttgctgtcc agtgcacaca tgtccatatt gcaaatggat	1900
acaagatata tggcaaggaa gccccatatt tctacaatga cactgtgaca	1950
ttcaagtgtt atagtggatt tactttgaag ggcagtagtc agattcgttg	2000
caaaagctgat aacacctggg atcctgaaat accagtttgt gaaaaagaaa	2050
catgccagca tgtgagacag agtcttcaag aacttccagc tggttcacgt	2100
gtggagctag ttaatacgtc ctgcccaagat gggtaaccagt tgactggaca	2150
tgcttatcag atgtgtcaag atgctgaaaa tggaaatttg ttcaaaaaga	2200
ttccactttg taaagtatt cactgtcacc ctcccaccagt gattgtcaat	2250
gggaagcaca cagggatgat ggcagaaaac tttctatatg gaaatgaagt	2300
ctcttatgaa tgtgaccaag gattctatct cctgggagag aaaaaattgc	2350
agtgcagaag tgattctaaa ggacatggat cttggagcgg gccttcccca	2400
cagtgcctac gatctcctcc tgtgactcgc tgccctaate cagaagtcaa	2450
acatgggtac aagctcaata aaacacattc tgcatattcc cacaatgaca	2500
tagtgtatgt tgactgcaat cctggcttca tcatgaatgg tagtcgctg	2550
attaggtgtc atactgataa cacatgggtg ccaggtgtgc caacttgtat	2600
gaaaaagacc ttcatagggt gtccacctcc gcctaagacc cctaaccggga	2650
accatactgg tggaaacata gctcgatttt ctccctggaat gtcaatcctg	2700
tacagctgtg accaaggcta cctgctggtg ggagaggcac tccttctttg	2750
cacacatgag ggaacctgga gccaacctgc ccctcattgt aaagaggtaa	2800
actgtagctc accagcagat atggatggaa tccagaaagg gctggaacca	2850
aggaaaaatgt atcagtatgg agctgttcta actctggagt gtgaagatgg	2900

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gtatatgctg gaaggcagtc cccagagcca gtgccaatcg gatcaccaat      2950
ggaaccctcc cctggcggtt tgcagatccc gttcacttgc tctgtcctt      3000
tgtggtattg ctgcaggttt gatacttctt accttcttga ttgtcattac      3050
cttatacgtg atatcaaaac acagagaacg caattattat acagatacaa      3100
gccagaaaaga agcttttcat ttagaagcac gagaagtata ttctgttgat      3150
ccatacaacc cagccagctg atcagaagac aaactgggtg gtgcctcatt      3200
gcttgggaatt cagcgaata ttgattagaa agaaactgct ctaatatcag      3250
caagtctctt tataatggcct caagatcaat gaaatgatgt cataagcgat      3300
cacttctctat atgcacttat tctcaagaag aacatcttta tggtaaagat      3350
gggagcccag tttcactgcc atatactctt caaggacttt ctgaagcctc      3400
acttatgaga tgcctgaagc caggccatgg ctataaacia ttacatggct      3450
ctaaaaagtt ttgccctttt taaggaaggc actaaaaaga gctgtcctgg      3500
tatctagacc catcttcttt ttgaaatcag catactcaat gttactatct      3550
gcttttggtt ataatgtggt ttttaattatc taaagtatga agcattttct      3600
ggggttatga tggccttacc tttattagga agtatggttt tattttgata      3650
gtagcttctc cctctggtgg tgtaatcat ttcattttta cccttactgt      3700
ttgagtttct ctcacattac tgtatatact ttgcccttcc ataatcactc      3750
agtgattgca atttgcacaa gtttttttaa attatgggaa tcaagattta      3800
atcctagaga tttggtgtac aattcaggct ttggatgttt ctttagcagt      3850
tttgtgataa gttctagtgt cttgtaaaat ttcacttaat aatgtgtaca      3900
ttagtcattc aataaattgt aattgtaaag aaaa                          3934

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<210> SEQ ID NO 12

<211> LENGTH: 1033

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 12

```

Met Gly Ala Ala Gly Leu Leu Gly Val Phe Leu Ala Leu Val Ala
 1          5          10          15
Pro Gly Val Leu Gly Ile Ser Cys Gly Ser Pro Pro Pro Ile Leu
 20          25          30
Asn Gly Arg Ile Ser Tyr Tyr Ser Thr Pro Ile Ala Val Gly Thr
 35          40          45
Val Ile Arg Tyr Ser Cys Ser Gly Thr Phe Arg Leu Ile Gly Glu
 50          55          60
Lys Ser Leu Leu Cys Ile Thr Lys Asp Lys Val Asp Gly Thr Trp
 65          70          75
Asp Lys Pro Ala Pro Lys Cys Glu Tyr Phe Asn Lys Tyr Ser Ser
 80          85          90
Cys Pro Glu Pro Ile Val Pro Gly Gly Tyr Lys Ile Arg Gly Ser
 95          100         105
Thr Pro Tyr Arg His Gly Asp Ser Val Thr Phe Ala Cys Lys Thr
 110         115         120
Asn Phe Ser Met Asn Gly Asn Lys Ser Val Trp Cys Gln Ala Asn
 125         130         135
Asn Met Trp Gly Pro Thr Arg Leu Pro Thr Cys Val Ser Val Phe
 140         145         150

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Pro	Leu	Glu	Cys	Pro	Ala	Leu	Pro	Met	Ile	His	Asn	Gly	His	His
				155					160					165
Thr	Ser	Glu	Asn	Val	Gly	Ser	Ile	Ala	Pro	Gly	Leu	Ser	Val	Thr
				170					175					180
Tyr	Ser	Cys	Glu	Ser	Gly	Tyr	Leu	Leu	Val	Gly	Glu	Lys	Ile	Ile
				185					190					195
Asn	Cys	Leu	Ser	Ser	Gly	Lys	Trp	Ser	Ala	Val	Pro	Pro	Thr	Cys
				200					205					210
Glu	Glu	Ala	Arg	Cys	Lys	Ser	Leu	Gly	Arg	Phe	Pro	Asn	Gly	Lys
				215					220					225
Val	Lys	Glu	Pro	Pro	Ile	Leu	Arg	Val	Gly	Val	Thr	Ala	Asn	Phe
				230					235					240
Phe	Cys	Asp	Glu	Gly	Tyr	Arg	Leu	Gln	Gly	Pro	Pro	Ser	Ser	Arg
				245					250					255
Cys	Val	Ile	Ala	Gly	Gln	Gly	Val	Ala	Trp	Thr	Lys	Met	Pro	Val
				260					265					270
Cys	Glu	Glu	Ile	Phe	Cys	Pro	Ser	Pro	Pro	Pro	Ile	Leu	Asn	Gly
				275					280					285
Arg	His	Ile	Gly	Asn	Ser	Leu	Ala	Asn	Val	Ser	Tyr	Gly	Ser	Ile
				290					295					300
Val	Thr	Tyr	Thr	Cys	Asp	Pro	Asp	Pro	Glu	Glu	Gly	Val	Asn	Phe
				305					310					315
Ile	Leu	Ile	Gly	Glu	Ser	Thr	Leu	Arg	Cys	Thr	Val	Asp	Ser	Gln
				320					325					330
Lys	Thr	Gly	Thr	Trp	Ser	Gly	Pro	Ala	Pro	Arg	Cys	Glu	Leu	Ser
				335					340					345
Thr	Ser	Ala	Val	Gln	Cys	Pro	His	Pro	Gln	Ile	Leu	Arg	Gly	Arg
				350					355					360
Met	Val	Ser	Gly	Gln	Lys	Asp	Arg	Tyr	Thr	Tyr	Asn	Asp	Thr	Val
				365					370					375
Ile	Phe	Ala	Cys	Met	Phe	Gly	Phe	Thr	Leu	Lys	Gly	Ser	Lys	Gln
				380					385					390
Ile	Arg	Cys	Asn	Ala	Gln	Gly	Thr	Trp	Glu	Pro	Ser	Ala	Pro	Val
				395					400					405
Cys	Glu	Lys	Glu	Cys	Gln	Ala	Pro	Pro	Asn	Ile	Leu	Asn	Gly	Gln
				410					415					420
Lys	Glu	Asp	Arg	His	Met	Val	Arg	Phe	Asp	Pro	Gly	Thr	Ser	Ile
				425					430					435
Lys	Tyr	Ser	Cys	Asn	Pro	Gly	Tyr	Val	Leu	Val	Gly	Glu	Glu	Ser
				440					445					450
Ile	Gln	Cys	Thr	Ser	Glu	Gly	Val	Trp	Thr	Pro	Pro	Val	Pro	Gln
				455					460					465
Cys	Lys	Val	Ala	Ala	Cys	Glu	Ala	Thr	Gly	Arg	Gln	Leu	Leu	Thr
				470					475					480
Lys	Pro	Gln	His	Gln	Phe	Val	Arg	Pro	Asp	Val	Asn	Ser	Ser	Cys
				485					490					495
Gly	Glu	Gly	Tyr	Lys	Leu	Ser	Gly	Ser	Val	Tyr	Gln	Glu	Cys	Gln
				500					505					510
Gly	Thr	Ile	Pro	Trp	Phe	Met	Glu	Ile	Arg	Leu	Cys	Lys	Glu	Ile
				515					520					525
Thr	Cys	Pro	Pro	Pro	Pro	Val	Ile	Tyr	Asn	Gly	Ala	His	Thr	Gly
				530					535					540

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Ser	Ser	Leu	Glu	Asp	Phe	Pro	Tyr	Gly	Thr	Thr	Val	Thr	Tyr	Thr	545	550	555
Cys	Asn	Pro	Gly	Pro	Glu	Arg	Gly	Val	Glu	Phe	Ser	Leu	Ile	Gly	560	565	570
Glu	Ser	Thr	Ile	Arg	Cys	Thr	Ser	Asn	Asp	Gln	Glu	Arg	Gly	Thr	575	580	585
Trp	Ser	Gly	Pro	Ala	Pro	Leu	Cys	Lys	Leu	Ser	Leu	Leu	Ala	Val	590	595	600
Gln	Cys	Ser	His	Val	His	Ile	Ala	Asn	Gly	Tyr	Lys	Ile	Ser	Gly	605	610	615
Lys	Glu	Ala	Pro	Tyr	Phe	Tyr	Asn	Asp	Thr	Val	Thr	Phe	Lys	Cys	620	625	630
Tyr	Ser	Gly	Phe	Thr	Leu	Lys	Gly	Ser	Ser	Gln	Ile	Arg	Cys	Lys	635	640	645
Ala	Asp	Asn	Thr	Trp	Asp	Pro	Glu	Ile	Pro	Val	Cys	Glu	Lys	Glu	650	655	660
Thr	Cys	Gln	His	Val	Arg	Gln	Ser	Leu	Gln	Glu	Leu	Pro	Ala	Gly	665	670	675
Ser	Arg	Val	Glu	Leu	Val	Asn	Thr	Ser	Cys	Gln	Asp	Gly	Tyr	Gln	680	685	690
Leu	Thr	Gly	His	Ala	Tyr	Gln	Met	Cys	Gln	Asp	Ala	Glu	Asn	Gly	695	700	705
Ile	Trp	Phe	Lys	Lys	Ile	Pro	Leu	Cys	Lys	Val	Ile	His	Cys	His	710	715	720
Pro	Pro	Pro	Val	Ile	Val	Asn	Gly	Lys	His	Thr	Gly	Met	Met	Ala	725	730	735
Glu	Asn	Phe	Leu	Tyr	Gly	Asn	Glu	Val	Ser	Tyr	Glu	Cys	Asp	Gln	740	745	750
Gly	Phe	Tyr	Leu	Leu	Gly	Glu	Lys	Lys	Leu	Gln	Cys	Arg	Ser	Asp	755	760	765
Ser	Lys	Gly	His	Gly	Ser	Trp	Ser	Gly	Pro	Ser	Pro	Gln	Cys	Leu	770	775	780
Arg	Ser	Pro	Pro	Val	Thr	Arg	Cys	Pro	Asn	Pro	Glu	Val	Lys	His	785	790	795
Gly	Tyr	Lys	Leu	Asn	Lys	Thr	His	Ser	Ala	Tyr	Ser	His	Asn	Asp	800	805	810
Ile	Val	Tyr	Val	Asp	Cys	Asn	Pro	Gly	Phe	Ile	Met	Asn	Gly	Ser	815	820	825
Arg	Val	Ile	Arg	Cys	His	Thr	Asp	Asn	Thr	Trp	Val	Pro	Gly	Val	830	835	840
Pro	Thr	Cys	Met	Lys	Lys	Ala	Phe	Ile	Gly	Cys	Pro	Pro	Pro	Pro	845	850	855
Lys	Thr	Pro	Asn	Gly	Asn	His	Thr	Gly	Gly	Asn	Ile	Ala	Arg	Phe	860	865	870
Ser	Pro	Gly	Met	Ser	Ile	Leu	Tyr	Ser	Cys	Asp	Gln	Gly	Tyr	Leu	875	880	885
Leu	Val	Gly	Glu	Ala	Leu	Leu	Leu	Cys	Thr	His	Glu	Gly	Thr	Trp	890	895	900
Ser	Gln	Pro	Ala	Pro	His	Cys	Lys	Glu	Val	Asn	Cys	Ser	Ser	Pro	905	910	915
Ala	Asp	Met	Asp	Gly	Ile	Gln	Lys	Gly	Leu	Glu	Pro	Arg	Lys	Met	920	925	930
Tyr	Gln	Tyr	Gly	Ala	Val	Val	Thr	Leu	Glu	Cys	Glu	Asp	Gly	Tyr			

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	935		940		945									
Met	Leu	Glu	Gly	Ser	Pro	Gln	Ser	Gln	Cys	Gln	Ser	Asp	His	Gln
				950					955					960
Trp	Asn	Pro	Pro	Leu	Ala	Val	Cys	Arg	Ser	Arg	Ser	Leu	Ala	Pro
				965					970					975
Val	Leu	Cys	Gly	Ile	Ala	Ala	Gly	Leu	Ile	Leu	Leu	Thr	Phe	Leu
				980					985					990
Ile	Val	Ile	Thr	Leu	Tyr	Val	Ile	Ser	Lys	His	Arg	Glu	Arg	Asn
				995					1000					1005
Tyr	Tyr	Thr	Asp	Thr	Ser	Gln	Lys	Glu	Ala	Phe	His	Leu	Glu	Ala
				1010					1015					1020
Arg	Glu	Val	Tyr	Ser	Val	Asp	Pro	Tyr	Asn	Pro	Ala	Ser		
				1025					1030					

<210> SEQ ID NO 13

<211> LENGTH: 2978

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 13

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caaacggttcc caaatcttcc cagtcggctt gcagagactc cttgctccca      50
ggagataaacc agaagctgca tcttattgac agatggcat cacattggtg      100
agctggagtc atcagattgt ggggcccgga gtgaggctga agggagtgga      150
tcagagcaact gcctgagagt cacctctact ttcctgtac cgetgcctgt      200
gagctgaagg ggctgaacca tacactcctt tttctacaac cagcttgcac      250
ttttctgcc cacaatgagc ggggaatcaa tgaatttcag cgatgttttc      300
gactccagtg aagattatct tgtgtcagtc aatacttcat attactcagt      350
tgattctgag atgttactgt gctccttgca ggaggtcagg cagttctcca      400
ggctatttgt accgattgcc tactccttga tctgtgtctt tggcctctctg      450
gggaatatct tgggtggtgat cacctttgct ttttataaga aggccaggtc      500
tatgacagac gtctatctct tgaacatggc cattgcagac atcctctttg      550
ttcttactct cccattctgg gcagtgagtc atgccactgg tgcgtgggtt      600
ttcagcaatg ccacgtgcaa gttgctaaaa ggcactctat ccatcaactt      650
taactgctgg atgctgctcc tgacttgcat tagcatggac cggtagatcg      700
ccattgtaca ggcgactaag tcattccggc tccgatccag aacactaccg      750
cgacagaaaa tcatctgctt tgtgtgtggt gggctgtcag tcatcatctc      800
cagctcaact tttgtcttca accaaaaata caacacccaa ggcagcgatg      850
tctgtgaacc caagtaccag actgtctcgg agcccatcag gtggaagctg      900
ctgatgttgg ggettgagct actccttggg ttccttatcc ctttgatgtt      950
catgatattt tgttacagct tcattgtcaa aacctgggtg caagctcaga     1000
attctaaaag gcacaaagcc atccgtgtaa tcatagctgt ggtgcttgtg     1050
tttctggctt gtcagattcc tcataacatg gtcctgcttg tgacggctgc     1100
aaatttgggt aaaatgaacc gatcctgcca gagcgaaaag ctaattggct     1150
atacgaaaac tgtcacagaa gtctctggct tectgcactg ctgectgaac     1200
cctgtgctct acgcttttat tgggcagaag ttcagaaact actttctgaa     1250
gatcttgaag gacctgtggt gtgtgagaag gaagtacaag tcctcaggct     1300

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tctcctgtgc cgggaggtac tcagaaaaca tttctcgga gaccagtgag	1350
accgcagata acgacaatgc gtcgctcttc actatgtgat agaaagctga	1400
gtctccctaa ggcattgtgtg aaacatactc atagatgtta tgcaaaaaa	1450
agtctatggc caggtatgca tggaaaatgt gggaaattaag caaaatcaag	1500
caagcctctc tcctgcggga cttaacgtgc tcatgggctg tgtgatctct	1550
tcagggtggg gtggtctctg ataggtagca tttccagca ctttgcaagg	1600
aatgttttgt agctctaggg tatatatccg cctggcattt cacaaaacag	1650
cctttgggaa atgctgaatt aaagtgaatt gttgacaaat gtaaacattt	1700
tcagaaatat tcatgaagcg gtcacagatc acagtgtctt ttggttacag	1750
cacaaaatga tggcagtggt ttgaaaaact aaaacagaaa aaaaaatgga	1800
agccaacaca tcaactcattt taggcaaatg ttaaacatt tttatctatc	1850
agaatgttta ttggtgctgg ttataagcag caggattggc cggctagtgt	1900
ttcctctcat ttccctttga tacagtcaac aagcctgacc ctgtaaaatg	1950
gaggtggaaa gacaagctca agtgttcaca acctggaagt gcttcgggaa	2000
gaaggggaca atggcagaac aggtgttggg gacaattgtc accaattgga	2050
taaagcagct caggtttag tgggccatta gaaaactgtc ggtttgcttt	2100
gatttccctg ggagctgttc tctgtcgtga gtgtctcttg tctaaacgtc	2150
cattaagctg agagtgtat gaagacagga tctagaataa tcttgctcac	2200
agctgtgtc tgagtgccta gcgagttcc agcaaacaaa atggactcaa	2250
gagagatttg attaataaat cgtaatgaag ttggggttta ttgtacagtt	2300
taaaatgtta gatgttttta attttttaa taaatggaat actttttttt	2350
tttttaaaga aagcaacttt actgagacaa tgtagaaga agttttgttc	2400
cgtttcttta atgtggttga agagcaatgt gtggctgaag acttttgta	2450
tgaggagctg cagattagct aggggacagc tggaaattatg ctggcttctg	2500
ataattattt taaaggggtc tgaatttgt gatggaatca gattttaaca	2550
gctctcttca atgacataga aagttcatgg aactcatgtt tttaaagggc	2600
tatgtaaata tatgaacatt agaaaaatag caacttgtgt tacaaaaata	2650
caaacacatg ttaggaaggt actgtcatgg gctaggcatg gtggctcaca	2700
cctgtaatcc cagcattttg ggaagctaag atgggtggat cacttgaggt	2750
caggagtttg agaccagcct ggccaacatg gcgaaacccc tctctactaa	2800
aaatacaaaa atttgccagg cgtgggtggcg ggtgctgta atcccagcta	2850
cttgggaggc tgaggcaaga gaatcgcttg aaccaggag gcagaggttg	2900
cagtgagccg agatcgtgcc attgcactcc agcctgggtg acagagcgag	2950
actccatctc aaaaaaaaaa aaaaaaaaaa	2978

<210> SEQ ID NO 14

<211> LENGTH: 374

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 14

Met Ser Gly Glu Ser Met Asn Phe Ser Asp Val Phe Asp Ser Ser
 1 5 10 15

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Glu Asp Tyr Phe Val Ser Val Asn Thr Ser Tyr Tyr Ser Val Asp
 20 25 30
 Ser Glu Met Leu Leu Cys Ser Leu Gln Glu Val Arg Gln Phe Ser
 35 40 45
 Arg Leu Phe Val Pro Ile Ala Tyr Ser Leu Ile Cys Val Phe Gly
 50 55 60
 Leu Leu Gly Asn Ile Leu Val Val Ile Thr Phe Ala Phe Tyr Lys
 65 70 75
 Lys Ala Arg Ser Met Thr Asp Val Tyr Leu Leu Asn Met Ala Ile
 80 85 90
 Ala Asp Ile Leu Phe Val Leu Thr Leu Pro Phe Trp Ala Val Ser
 95 100 105
 His Ala Thr Gly Ala Trp Val Phe Ser Asn Ala Thr Cys Lys Leu
 110 115 120
 Leu Lys Gly Ile Tyr Ala Ile Asn Phe Asn Cys Gly Met Leu Leu
 125 130 135
 Leu Thr Cys Ile Ser Met Asp Arg Tyr Ile Ala Ile Val Gln Ala
 140 145 150
 Thr Lys Ser Phe Arg Leu Arg Ser Arg Thr Leu Pro Arg Thr Lys
 155 160 165
 Ile Ile Cys Leu Val Val Trp Gly Leu Ser Val Ile Ile Ser Ser
 170 175 180
 Ser Thr Phe Val Phe Asn Gln Lys Tyr Asn Thr Gln Gly Ser Asp
 185 190 195
 Val Cys Glu Pro Lys Tyr Gln Thr Val Ser Glu Pro Ile Arg Trp
 200 205 210
 Lys Leu Leu Met Leu Gly Leu Glu Leu Leu Phe Gly Phe Phe Ile
 215 220 225
 Pro Leu Met Phe Met Ile Phe Cys Tyr Thr Phe Ile Val Lys Thr
 230 235 240
 Leu Val Gln Ala Gln Asn Ser Lys Arg His Lys Ala Ile Arg Val
 245 250 255
 Ile Ile Ala Val Val Leu Val Phe Leu Ala Cys Gln Ile Pro His
 260 265 270
 Asn Met Val Leu Leu Val Thr Ala Ala Asn Leu Gly Lys Met Asn
 275 280 285
 Arg Ser Cys Gln Ser Glu Lys Leu Ile Gly Tyr Thr Lys Thr Val
 290 295 300
 Thr Glu Val Leu Ala Phe Leu His Cys Cys Leu Asn Pro Val Leu
 305 310 315
 Tyr Ala Phe Ile Gly Gln Lys Phe Arg Asn Tyr Phe Leu Lys Ile
 320 325 330
 Leu Lys Asp Leu Trp Cys Val Arg Arg Lys Tyr Lys Ser Ser Gly
 335 340 345
 Phe Ser Cys Ala Gly Arg Tyr Ser Glu Asn Ile Ser Arg Gln Thr
 350 355 360
 Ser Glu Thr Ala Asp Asn Asp Asn Ala Ser Ser Phe Thr Met
 365 370

<210> SEQ ID NO 15

<211> LENGTH: 1531

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 15

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agtcacagag ggaacacaga gcctagttgt aaacggacag agacgagagg      50
ggcaagggag gacagtggat gacaggaag acgagtgggg gcagagctgc      100
tcaggacat ggctgaggcc atcacctatg cagatctgag gtttgtgaag      150
gctcccctga agaagagcat ctccagcccg ttaggacagg acccaggggg      200
tgatgatgat ggggaaatca cctacgagaa tgttcaagtg cccgcagtcc      250
taggggtgcc ctcaagcttg gcttctctg tactagggga caaagcagcg      300
gtcaagtccg agcagccaac tgcgtcctgg agagccgtga cgtcaccagc      350
tgtcggggcg atttcccct gccgcacaac ctgctcgcga tacctcctgc      400
tcggcctgct cctcacctgc ctgctgtag gaggaccgc catctgcctg      450
ggagtgcct atctgcaggt gtctcagcag ctccagcaga cgaacaggg      500
tctggaagtc actaacagca gctgaggca gcagctccg ctcaagataa      550
cgcagctggg acagagtga gaggatctgc aggggtccag gagagagctg      600
gcgcagagtc aggaagcact acaggtggaa cagagggctc atcaggcggc      650
cgaagggcag ctacaggcct gccaggcaga cagacagaag acgaaggaga      700
ccttgcaaag tgaggagcaa cagaggaggg ccttgagca gaagctgagc      750
aacatggaga acagactgaa gccctcttc acatcggct cagcagacac      800
ctgctgtccg tcgggatgga taatgcatca gaaaagctgc ttttacatct      850
cacttacttc aaaaaattgg caggagagcc aaaaacaatg tgaaactctg      900
tcttccaagc tggccacatt cagtgaatt tatccacaat cacactctta      950
ctactctta aattcactgt tgccaaatgg tggttcaggg aattcatatt     1000
ggactggcct cagctctaac aaggattgga agttgactga tgatacacia     1050
cgcactagga cttatgctca aagctcaaaa tgtaacaagg tacataaaac     1100
ttggtcatgg tggacactgg agtcagagtc atgtagaagt tctcttccct     1150
acatctgtga gatgacagct ttcaggtttc cagattagga cagtcctttg     1200
cactgagttg aactcactgc caacaagaac ctgtgcccct ccttctaac     1250
ctgaggcctg gggttctca gaccatctcc ttcattctgg gcagtgccag     1300
ccaccggctg acccacacct gacactcca gccagtctgc tgctgtctcc     1350
ctcttctga aactggactg ttctctggaa aagggtgaag ccacctctag     1400
aagggacttt ggctcccc caagaacttc ccatggtaga atgggggtggg     1450
ggaggagggc gcacgggctg agcggatagg ggcggcccgg agccagccag     1500
gcagttttat tgaatcttt ttaataaatt g                          1531

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<210> SEQ ID NO 16

<211> LENGTH: 359

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 16

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Met Ala Glu Ala Ile Thr Tyr Ala Asp Leu Arg Phe Val Lys Ala
  1           5           10           15
Pro Leu Lys Lys Ser Ile Ser Ser Arg Leu Gly Gln Asp Pro Gly
           20           25           30
Ala Asp Asp Asp Gly Glu Ile Thr Tyr Glu Asn Val Gln Val Pro

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-continued

	35		40		45
Ala Val Leu Gly Val Pro Ser Ser Leu Ala Ser Ser Val Leu Gly	50		55		60
Asp Lys Ala Ala Val Lys Ser Glu Gln Pro Thr Ala Ser Trp Arg	65		70		75
Ala Val Thr Ser Pro Ala Val Gly Arg Ile Leu Pro Cys Arg Thr	80		85		90
Thr Cys Leu Arg Tyr Leu Leu Leu Gly Leu Leu Leu Thr Cys Leu	95		100		105
Leu Leu Gly Val Thr Ala Ile Cys Leu Gly Val Arg Tyr Leu Gln	110		115		120
Val Ser Gln Gln Leu Gln Gln Thr Asn Arg Val Leu Glu Val Thr	125		130		135
Asn Ser Ser Leu Arg Gln Gln Leu Arg Leu Lys Ile Thr Gln Leu	140		145		150
Gly Gln Ser Ala Glu Asp Leu Gln Gly Ser Arg Arg Glu Leu Ala	155		160		165
Gln Ser Gln Glu Ala Leu Gln Val Glu Gln Arg Ala His Gln Ala	170		175		180
Ala Glu Gly Gln Leu Gln Ala Cys Gln Ala Asp Arg Gln Lys Thr	185		190		195
Lys Glu Thr Leu Gln Ser Glu Glu Gln Gln Arg Arg Ala Leu Glu	200		205		210
Gln Lys Leu Ser Asn Met Glu Asn Arg Leu Lys Pro Phe Phe Thr	215		220		225
Cys Gly Ser Ala Asp Thr Cys Cys Pro Ser Gly Trp Ile Met His	230		235		240
Gln Lys Ser Cys Phe Tyr Ile Ser Leu Thr Ser Lys Asn Trp Gln	245		250		255
Glu Ser Gln Lys Gln Cys Glu Thr Leu Ser Ser Lys Leu Ala Thr	260		265		270
Phe Ser Glu Ile Tyr Pro Gln Ser His Ser Tyr Tyr Phe Leu Asn	275		280		285
Ser Leu Leu Pro Asn Gly Gly Ser Gly Asn Ser Tyr Trp Thr Gly	290		295		300
Leu Ser Ser Asn Lys Asp Trp Lys Leu Thr Asp Asp Thr Gln Arg	305		310		315
Thr Arg Thr Tyr Ala Gln Ser Ser Lys Cys Asn Lys Val His Lys	320		325		330
Thr Trp Ser Trp Trp Thr Leu Glu Ser Glu Ser Cys Arg Ser Ser	335		340		345
Leu Pro Tyr Ile Cys Glu Met Thr Ala Phe Arg Phe Pro Asp	350		355		

<210> SEQ ID NO 17

<211> LENGTH: 1978

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 17

ggcacgaggg tccgcaagcc cggctgagag cgcgccatgg ggcaggcggg 50

ctgcaagggg ctctgcctgt cgctgttcga ctacaagacc gagaagtatg 100

tcatcgccaa gaacaagaag gtgggcctgc tgtaccggt gctgcaggcc 150

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tccatcctgg cgtacctggt cgtatgggtg ttcctgataa agaagggtta	200
ccaagacgtc gacacctccc tgcagagtgc tgtcatcacc aaagtcaagg	250
gcgtggcctt caccaacacc tcggatcttg ggcagcggat ctgggatgtc	300
gccgactaog tcattccage ccagggagag aacgtctttt ttgtggtcac	350
caacctgatt gtgaccccca accagcggca gaacgtctgt gctgagaatg	400
aaggcattcc tgatggcgcg tgetccaagg acagcgaactg ccacgctggg	450
gaagcgggta cagctggaaa cggagtgaag accggccgct gcctgaggag	500
agggaaacttg gccaggggca cctgtgagat ctttgccctgg tgcccgttgg	550
agacaagctc caggccggag gagccattcc tgaaggaggc cgaagacttc	600
accattttca taaagaacca catccgtttc cccaaattca acttctccaa	650
aaacaatgtg atggacgtca aggacagatc tttcctgaaa tcatgccact	700
ttggcccccga gaacctact tggcccatct tccgactggg ctccatcgtc	750
cgctgggccc ggagcgactt ccaggatata gccctgagag gtggcgtgat	800
aggaattaat attgaatgga actgtgatct tgataaagct gcctctgagt	850
gccaccctca ctattctttt agccgtctgg acaataaaact ttcaaagtct	900
gtctcctcog ggtacaactt cagatttgc agatattacc gagacgcagc	950
cggggtggag ttccgcaccc tgatgaaagc ctacgggatc cgctttgacg	1000
tgatgggtgaa cggcaagggt gctttcttct ggcacctggg actcatctac	1050
ctcatcaaaa agagagagtt ttaccgtgac aagaagtacg aggaagtgag	1100
gggcctagaa gacagttccc aggaggccga ggacgagcca tcggggctgg	1150
ggctatctga gcagctcaca tctgggcccag ggctgctggg gatgccggag	1200
cagcaggagc tgcaggagcc acccgaggcg aagcgtggaa gcagcagtca	1250
gaaggggaaac ggatctgtgt gccacagct cctggagccc cacaggagca	1300
cgtgaattgc ctctgcttac gttcaggccc tgtcctaaac ccagccgtct	1350
agcaccagct gatcccatgc ctttgggaat cccaggatgc tgcccaacgg	1400
gaaatttcta cattgggtgc tatcaatgcc acatcacagg gaccagccat	1450
cacagagcaa agtgacctcc acgtctgatg ctggggatcat caggacggac	1500
ccatcatggc tgtctttttg cccaccccc tgccgtcagt tcttctttc	1550
tccgtggctg gcttcccga ctagggaacg ggttgtaaat ggggaacatg	1600
acttctctcc ggagtcttg agcacctcag ctaaggaccg cagtgcctg	1650
tagagttcct agattacctc actgggaata gcattgtgcg tgtccggaaa	1700
agggctccat ttggttcag cccactcccc tctgcaagtg ccacagcttc	1750
cctcagagca tactctccag tggatccaag tactctctct cctaagaca	1800
ccaccttctc gccagctggt tgcccttagg ccagtacaca gaattaaagt	1850
gggggagatg gcagacgctt tctgggacct gcccaagata tgtattctct	1900
gacactctta tttggtcata aaacaataaa tgggtgcaat ttcaaaaaaa	1950
aaaaaaaaa aaaaaaaaaa aaaaaaaaa	1978

<210> SEQ ID NO 18

<211> LENGTH: 422

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 18

Met Gly Gln Ala Gly Cys Lys Gly Leu Cys Leu Ser Leu Phe Asp
 1 5 10 15
 Tyr Lys Thr Glu Lys Tyr Val Ile Ala Lys Asn Lys Lys Val Gly
 20 25 30
 Leu Leu Tyr Arg Leu Leu Gln Ala Ser Ile Leu Ala Tyr Leu Val
 35 40 45
 Val Trp Val Phe Leu Ile Lys Lys Gly Tyr Gln Asp Val Asp Thr
 50 55 60
 Ser Leu Gln Ser Ala Val Ile Thr Lys Val Lys Gly Val Ala Phe
 65 70 75
 Thr Asn Thr Ser Asp Leu Gly Gln Arg Ile Trp Asp Val Ala Asp
 80 85 90
 Tyr Val Ile Pro Ala Gln Gly Glu Asn Val Phe Phe Val Val Thr
 95 100 105
 Asn Leu Ile Val Thr Pro Asn Gln Arg Gln Asn Val Cys Ala Glu
 110 115 120
 Asn Glu Gly Ile Pro Asp Gly Ala Cys Ser Lys Asp Ser Asp Cys
 125 130 135
 His Ala Gly Glu Ala Val Thr Ala Gly Asn Gly Val Lys Thr Gly
 140 145 150
 Arg Cys Leu Arg Arg Gly Asn Leu Ala Arg Gly Thr Cys Glu Ile
 155 160 165
 Phe Ala Trp Cys Pro Leu Glu Thr Ser Ser Arg Pro Glu Glu Pro
 170 175 180
 Phe Leu Lys Glu Ala Glu Asp Phe Thr Ile Phe Ile Lys Asn His
 185 190 195
 Ile Arg Phe Pro Lys Phe Asn Phe Ser Lys Asn Asn Val Met Asp
 200 205 210
 Val Lys Asp Arg Ser Phe Leu Lys Ser Cys His Phe Gly Pro Lys
 215 220 225
 Asn His Tyr Cys Pro Ile Phe Arg Leu Gly Ser Ile Val Arg Trp
 230 235 240
 Ala Gly Ser Asp Phe Gln Asp Ile Ala Leu Arg Gly Gly Val Ile
 245 250 255
 Gly Ile Asn Ile Glu Trp Asn Cys Asp Leu Asp Lys Ala Ala Ser
 260 265 270
 Glu Cys His Pro His Tyr Ser Phe Ser Arg Leu Asp Asn Lys Leu
 275 280 285
 Ser Lys Ser Val Ser Ser Gly Tyr Asn Phe Arg Phe Ala Arg Tyr
 290 295 300
 Tyr Arg Asp Ala Ala Gly Val Glu Phe Arg Thr Leu Met Lys Ala
 305 310 315
 Tyr Gly Ile Arg Phe Asp Val Met Val Asn Gly Lys Gly Ala Phe
 320 325 330
 Phe Cys Asp Leu Val Leu Ile Tyr Leu Ile Lys Lys Arg Glu Phe
 335 340 345
 Tyr Arg Asp Lys Lys Tyr Glu Glu Val Arg Gly Leu Glu Asp Ser
 350 355 360
 Ser Gln Glu Ala Glu Asp Glu Ala Ser Gly Leu Gly Leu Ser Glu
 365 370 375
 Gln Leu Thr Ser Gly Pro Gly Leu Leu Gly Met Pro Glu Gln Gln

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380				385				390						
Glu	Leu	Gln	Glu	Pro	Pro	Glu	Ala	Lys	Arg	Gly	Ser	Ser	Ser	Gln
				395					400					405
Lys	Gly	Asn	Gly	Ser	Val	Cys	Pro	Gln	Leu	Leu	Glu	Pro	His	Arg
				410					415					420

Ser Thr

<210> SEQ ID NO 19
 <211> LENGTH: 1322
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 19

```

aactcattct gaagaggctg acgattttac tgtctcattt ttttcctttc      50
tccagaatgg gttctggggtg ggtccctctg gtggtggctc tgctagttaa      100
tctgacccca ctggattcct ccatgactca aggcacagac tctccagaag      150
atthttgtgat tcaggcaaag gctgactggt acttcaccaa cgggacagaa      200
aaggtgcagt ttgtggtcag attcatcttt aacttggagg agtatgtacg      250
tttcgacagt gatgtgggga tgtttgtggc attgaccaag ctggggcagc      300
cagatgctga gcagtggaac agccggctgg atctcttggg gaggagcaga      350
caggccgtgg atggggtctg tagacacaac tacaggctgg gcgcaccctt      400
cactgtgggg agaaaagtgc aaccagaggt gacagtgtac ccagagagga      450
ccccactcct gcaccagcat aatctgctgc actgctctgt gacaggcttc      500
tatccagggg atatcaagat caagtgggtc ctgaatgggc aggaggagag      550
agctggggtc atgtccactg gccctatcag gaatggagac tggacctttc      600
agactgtggt gatgctagaa atgactcctg aacttggaca tgtctacacc      650
tgccttctcg atcactccag cctgctgagc cctgtttctg tggagtggag      700
agctcagttc gaatattcct ggagaaagat gctgagtggc attgcagcct      750
tctactctgg gctaactctc cttctgggtg gaatcgtcat ccagetaagg      800
gctcagaaa gatatgtgag gacgcagatg tctggtaatg aggtctcaag      850
agctgttctg ctccctcagt catgctaagg tctcactaaa gcttgccttc      900
tctggagcct gaagtagtga tgagtgtct gggccctggg tgaggtaaag      950
gacattcatg aggtcaatgt tctgggaata actctcttcc ctgacacctg     1000
gaggagcccc aactgattct ggagctctgt gttctgagat catgcatctc     1050
ccaccatctc gcccttctcc cttctactgt tacatcatta atccccattg     1100
ccaagggcat tgtccagaaa ctccccctgag accttactcc tccagcccc     1150
aaatcattta cttttctgtg gtccagccct actcctataa gtcattgatct     1200
ccaaagcttt ctgtcttcca actgcagtct ccacagtctt cagaagacaa     1250
atgctcaggt agtcaactgt tccttttccac tgtttttaa aaccttttat     1300
tgtcaataaa aatggagata ca                                     1322

```

<210> SEQ ID NO 20
 <211> LENGTH: 273
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 20

-continued

Met Gly Ser Gly Trp Val Pro Trp Val Val Ala Leu Leu Val Asn
 1 5 10 15
 Leu Thr Arg Leu Asp Ser Ser Met Thr Gln Gly Thr Asp Ser Pro
 20 25 30
 Glu Asp Phe Val Ile Gln Ala Lys Ala Asp Cys Tyr Phe Thr Asn
 35 40 45
 Gly Thr Glu Lys Val Gln Phe Val Val Arg Phe Ile Phe Asn Leu
 50 55 60
 Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Met Phe Val Ala
 65 70 75
 Leu Thr Lys Leu Gly Gln Pro Asp Ala Glu Gln Trp Asn Ser Arg
 80 85 90
 Leu Asp Leu Leu Glu Arg Ser Arg Gln Ala Val Asp Gly Val Cys
 95 100 105
 Arg His Asn Tyr Arg Leu Gly Ala Pro Phe Thr Val Gly Arg Lys
 110 115 120
 Val Gln Pro Glu Val Thr Val Tyr Pro Glu Arg Thr Pro Leu Leu
 125 130 135
 His Gln His Asn Leu Leu His Cys Ser Val Thr Gly Phe Tyr Pro
 140 145 150
 Gly Asp Ile Lys Ile Lys Trp Phe Leu Asn Gly Gln Glu Glu Arg
 155 160 165
 Ala Gly Val Met Ser Thr Gly Pro Ile Arg Asn Gly Asp Trp Thr
 170 175 180
 Phe Gln Thr Val Val Met Leu Glu Met Thr Pro Glu Leu Gly His
 185 190 195
 Val Tyr Thr Cys Leu Val Asp His Ser Ser Leu Leu Ser Pro Val
 200 205 210
 Ser Val Glu Trp Arg Ala Gln Ser Glu Tyr Ser Trp Arg Lys Met
 215 220 225
 Leu Ser Gly Ile Ala Ala Phe Leu Leu Gly Leu Ile Phe Leu Leu
 230 235 240
 Val Gly Ile Val Ile Gln Leu Arg Ala Gln Lys Gly Tyr Val Arg
 245 250 255
 Thr Gln Met Ser Gly Asn Glu Val Ser Arg Ala Val Leu Leu Pro
 260 265 270

Gln Ser Cys

<210> SEQ ID NO 21
 <211> LENGTH: 2818
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

gctgccacct ctctagaggc acctggcggg gaggccttca acataagaca 50
 gtgaccagtc tggtagactca cagccggcac agccatgaac taccgctaa 100
 cgctggaaat ggacctcgag aacctggagg acctgttctg ggaactggac 150
 agattggaca actataacga cacctccctg gtgaaaaatc atctctgccc 200
 tgccacagag ggtcccctca tggcctcctt caaggccgtg ttcgtgcccc 250
 tggcctacag cctcatcttc ctctctggcg tgatcggcaa cgctctggtg 300
 ctggtgatcc tggagcggca ccggcagaca cgcagttcca cggagacctt 350

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cctgttccac ctggccgtgg ccgacctcct gctggttctt atcttgcctt	400
ttgccgtggc cgagggtctt gtgggtggg tcttggggac ctctctctgc	450
aaaactgtga ttgccctgca caaagtcaac ttctactgca gcagcctgct	500
cctggcctgc atcgccgtgg accgctacct ggccattgtc cagcgcctcc	550
atgcctaccg ccaccgcgcg ctctcttcca tccacatcac ctgtgggacc	600
atctggctgg tgggcttctt ccttgccctg ccagagattc tcttgcctaa	650
agtcagccaa ggccatcaca acaactcctt gccacgttgc accttctccc	700
aagagaacca agcagaaaac catgcctggg tcacctcccg attctcttac	750
catgtggcgg gattcctgct gcccatgctg gtgatgggct ggtgctacgt	800
gggggtagtg cacagggtgc gccaggccca gcggcgcctt cagcggcaga	850
aggcagtcag ggtggccatc ctgggtgacaa gcattctctt cctctgctgg	900
tcacctacc acatcgctat ctctctggac accctggcga ggctgaagge	950
cgtggacaat acctgcaagc tgaatggctt tctcccctg gccatcacca	1000
tgtgtgagtt cctgggctg gcccaatgct gctcaacct catgctctac	1050
actttcgcg gcgtgaagtt ccgcatgac ctgtcggcgc tctgaccaa	1100
gctgggctgt accggccctg cctcctgtg ccagctctt cctagctggc	1150
gcaggagcag tctctctgag tcagagaatg ccacctctt caccacgttc	1200
taggtcccag tgtcccctt tattgtgctt ttctctggg gcaggcagtg	1250
atgctggatg ctcttccaa caggagctgg gatcctaagg gctcaccgtg	1300
gctaagagtg tcctaggagt atctctattt ggggtagcta gaggaaccaa	1350
ccccattctt agaacatccc tggcagctt tctgcccggc ctggggctag	1400
gctggagccc agggagcggg aagcagctcg aaggcacagt gaaggctgtc	1450
cttaccatc tgcaccccc tgggctgaga gaacctcacg cacctcccat	1500
cctaatac ccaatgctcaa gaaacaactt ctacttctgc ccttgccaac	1550
ggagagcgcg tggccctccc agaacacact ccatcagctt aggggctgct	1600
gacctccaca gcttcccctc tctctctctg cccacctgtc aaacaaagcc	1650
agaagctgag caccagggga tgagtggagg ttaaggctga ggaaaggcca	1700
gctggcagca gagtgggct tcggacaact cagtcctaa aaacacagac	1750
attctgccag gcccccaagc ctgcagtcatt cttgaccaag caggaagctc	1800
agactggttg agttcaggta gctgcccctg gctctgaccg aaacagcgtt	1850
gggtccacc catgtcaccg gatcctgggt ggtctgcagg cagggctgac	1900
tctaggtgcc cttggaggcc agccagtgac ctgaggaagc gtgaaggccg	1950
agaagcaaga aagaaacccg acagagggaa gaaaagagct ttcttcccga	2000
acccaagga gggagatgga tcaatcaaac ccggctgtcc cctccgccc	2050
ggcagatgg ggtgggggga gaactcctag ggtgctggg tccaggggat	2100
gggaggtgtt gggcattgat ggggaaggag gctgcttctt cccctcctca	2150
ctcccttccc ataagctata gaccgagga aactcagagt cggaacggag	2200
aaagtggtg tggaaagggc ccgtgggagt catctcaacc atcccctccg	2250
ttggcatcac cttaggcagg gaagtgtgaa aaacacactg aggcaggaac	2300
tcccaggccc aggaagcctg gccctgcccc cgtgaggatg tcaactcagat	2350

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ggaaccgcag gaagctgctc cgtgcttggt tgctcacctg ggggtgtggga      2400
ggcccgcocg gcagttctgg gtgctcccta ccacctcccc agcctttgat      2450
caggtgggga gtcagggacc cctgcccttg tccactcaa gccaaagcagc      2500
caagctcctt gggaggcccc actggggaaa taacagctgt ggctcacgtg      2550
agagtgtctt cacggcagga caacgagaaa gccctaagac gtcccttttt      2600
tctctgagta tctcctcgca agctgggtaa tcgatgggga gtctgaagca      2650
gatgcaaaga ggcagaggat ggattttgaa ttttcttttt aataaaaagg      2700
cacctataaa acaggtcaat acagtacagg cagcacagag acccccggaa      2750
caagcctaaa aattgtttca aaataaaaac caagaagatg tcttcaaaaa      2800
aaaaaaaaaa aaaaaaaaaa      2818

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<210> SEQ ID NO 22

<211> LENGTH: 372

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 22

```

Met Asn Tyr Pro Leu Thr Leu Glu Met Asp Leu Glu Asn Leu Glu
  1          5          10          15
Asp Leu Phe Trp Glu Leu Asp Arg Leu Asp Asn Tyr Asn Asp Thr
          20          25          30
Ser Leu Val Glu Asn His Leu Cys Pro Ala Thr Glu Gly Pro Leu
          35          40          45
Met Ala Ser Phe Lys Ala Val Phe Val Pro Val Ala Tyr Ser Leu
          50          55          60
Ile Phe Leu Leu Gly Val Ile Gly Asn Val Leu Val Leu Val Ile
          65          70          75
Leu Glu Arg His Arg Gln Thr Arg Ser Ser Thr Glu Thr Phe Leu
          80          85          90
Phe His Leu Ala Val Ala Asp Leu Leu Leu Val Phe Ile Leu Pro
          95          100          105
Phe Ala Val Ala Glu Gly Ser Val Gly Trp Val Leu Gly Thr Phe
          110          115          120
Leu Cys Lys Thr Val Ile Ala Leu His Lys Val Asn Phe Tyr Cys
          125          130          135
Ser Ser Leu Leu Leu Ala Cys Ile Ala Val Asp Arg Tyr Leu Ala
          140          145          150
Ile Val His Ala Val His Ala Tyr Arg His Arg Arg Leu Leu Ser
          155          160          165
Ile His Ile Thr Cys Gly Thr Ile Trp Leu Val Gly Phe Leu Leu
          170          175          180
Ala Leu Pro Glu Ile Leu Phe Ala Lys Val Ser Gln Gly His His
          185          190          195
Asn Asn Ser Leu Pro Arg Cys Thr Phe Ser Gln Glu Asn Gln Ala
          200          205          210
Glu Thr His Ala Trp Phe Thr Ser Arg Phe Leu Tyr His Val Ala
          215          220          225
Gly Phe Leu Leu Pro Met Leu Val Met Gly Trp Cys Tyr Val Gly
          230          235          240
Val Val His Arg Leu Arg Gln Ala Gln Arg Arg Pro Gln Arg Gln
          245          250          255

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Lys Ala Val Arg Val Ala Ile Leu Val Thr Ser Ile Phe Phe Leu
 260 265 270

Cys Trp Ser Pro Tyr His Ile Val Ile Phe Leu Asp Thr Leu Ala
 275 280 285

Arg Leu Lys Ala Val Asp Asn Thr Cys Lys Leu Asn Gly Ser Leu
 290 295 300

Pro Val Ala Ile Thr Met Cys Glu Phe Leu Gly Leu Ala His Cys
 305 310 315

Cys Leu Asn Pro Met Leu Tyr Thr Phe Ala Gly Val Lys Phe Arg
 320 325 330

Ser Asp Leu Ser Arg Leu Leu Thr Lys Leu Gly Cys Thr Gly Pro
 335 340 345

Ala Ser Leu Cys Gln Leu Phe Pro Ser Trp Arg Arg Ser Ser Leu
 350 355 360

Ser Glu Ser Glu Asn Ala Thr Ser Leu Thr Thr Phe
 365 370

<210> SEQ ID NO 23

<211> LENGTH: 1529

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 23

```

agtggctcta ctttcagaag aaagtgtctc tcttcctgct taaacctctg          50
tctctgacgg tccctgccaa tcgctctggt cgaccccaac aactaggag          100
gacagacaca ggctccaaac tccactaacc agagctgtga ttgtgcccg          150
tgagtggact gcgttgtcag ggagtgtgtg ctccatcctc gggagaatcc          200
aagcaggacc gccatggagg aaggtaata ttcagagatc gaggagcttc          250
ccaggaggcg gtgttcagg cgtgggactc agatcgtgct gctggggctg          300
gtgaccgccc ctctgtgggc tgggctgctg actctgcttc tcctgtggca          350
ctgggacacc acacagagtc taaaacagct ggaagagagg gctgcccgga          400
acgtctctca agtttccaag aacttgaaa gccaccacgg tgaccagatg          450
gcgcagaaat cccagtccac gcagatttca caggaactgg aggaacttcg          500
agctgaacag cagagattga aatctcagga cttggagctg tcctggaacc          550
tgaacgggct tcaagcagat ctgagcagct tcaagtccca ggaattgaac          600
gagaggaacg aagcttcaga tttgctggaa agactccggg aggaggtgac          650
aaagctaagg atggagtgc aggtgtccag cggctttgtg tgcaaacagt          700
gccctgaaaa gtggatcaac ttccaacgga agtgctacta cttcggcaag          750
ggcaccaagc agtgggtcca cggccggtat gcctgtgacg acatggaagg          800
gcagctggtc agcatccaca gcccgaggga gcaggacttc ctgaccaagc          850
atgccagcca caccggetcc tggattggcc ttcggaactt ggacctgaag          900
ggagagttta tctgggtgga tgggagccat gtggactaca gcaactgggc          950
tccaggggag cccaccagcc ggagccaggg cgaggactgc gtgatgatgc          1000
ggggctccgg tcgctggacc gacgccttct gcgaccgtaa gctgggcgccc          1050
tgggtgtgcg accggctggc cacatgcacg ccgccagcca gcgaaggttc          1100
cgcgagatcc atgggacctg attcaagacc agacctgac ggccgcctgc          1150

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```

ccaccccctc tgcacctctc cactcttgag catggatata gccaggccca      1200
gagcaagacc ctgaagaccc ccaaccacgg cctaaaagcc tctttgtggc      1250
tgaaaggctc ctgtgacatt ttctgccacc caaacggagg cagctgacac      1300
atctcccgcct cctctatggc cctgccttc ccaggagtac accccaacag      1350
caccctctcc agatggggagt gcccccaaca gcacctctc cagatgagag      1400
ttacacccca acagcacctc ctccagatgc agccccatct cctcagcacc      1450
ccaggacctg agtatcccca gctcagggtg gtgagtcctc ctgtccagcc      1500
tgcatacaata aaatggggca gtgatggcc      1529

```

<210> SEQ ID NO 24

<211> LENGTH: 321

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 24

```

Met Glu Glu Gly Gln Tyr Ser Glu Ile Glu Glu Leu Pro Arg Arg
 1                               10                          15
Arg Cys Cys Arg Arg Gly Thr Gln Ile Val Leu Leu Gly Leu Val
                20                          25                          30
Thr Ala Ala Leu Trp Ala Gly Leu Leu Thr Leu Leu Leu Trp
                35                          40                          45
His Trp Asp Thr Thr Gln Ser Leu Lys Gln Leu Glu Glu Arg Ala
                50                          55                          60
Ala Arg Asn Val Ser Gln Val Ser Lys Asn Leu Glu Ser His His
                65                          70                          75
Gly Asp Gln Met Ala Gln Lys Ser Gln Ser Thr Gln Ile Ser Gln
                80                          85                          90
Glu Leu Glu Glu Leu Arg Ala Glu Gln Gln Arg Leu Lys Ser Gln
                95                          100                         105
Asp Leu Glu Leu Ser Trp Asn Leu Asn Gly Leu Gln Ala Asp Leu
                110                         115                         120
Ser Ser Phe Lys Ser Gln Glu Leu Asn Glu Arg Asn Glu Ala Ser
                125                         130                         135
Asp Leu Leu Glu Arg Leu Arg Glu Glu Val Thr Lys Leu Arg Met
                140                         145                         150
Glu Leu Gln Val Ser Ser Gly Phe Val Cys Asn Thr Cys Pro Glu
                155                         160                         165
Lys Trp Ile Asn Phe Gln Arg Lys Cys Tyr Tyr Phe Gly Lys Gly
                170                         175                         180
Thr Lys Gln Trp Val His Ala Arg Tyr Ala Cys Asp Asp Met Glu
                185                         190                         195
Gly Gln Leu Val Ser Ile His Ser Pro Glu Glu Gln Asp Phe Leu
                200                         205                         210
Thr Lys His Ala Ser His Thr Gly Ser Trp Ile Gly Leu Arg Asn
                215                         220                         225
Leu Asp Leu Lys Gly Glu Phe Ile Trp Val Asp Gly Ser His Val
                230                         235                         240
Asp Tyr Ser Asn Trp Ala Pro Gly Glu Pro Thr Ser Arg Ser Gln
                245                         250                         255
Gly Glu Asp Cys Val Met Met Arg Gly Ser Gly Arg Trp Thr Asp
                260                         265                         270
Ala Phe Cys Asp Arg Lys Leu Gly Ala Trp Val Cys Asp Arg Leu

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275					280					285				
Ala	Thr	Cys	Thr	Pro	Pro	Ala	Ser	Glu	Gly	Ser	Ala	Glu	Ser	Met
				290					295					300
Gly	Pro	Asp	Ser	Arg	Pro	Asp	Pro	Asp	Gly	Arg	Leu	Pro	Thr	Pro
				305					310					315
Ser	Ala	Pro	Leu	His	Ser									
				320										

<210> SEQ ID NO 25

<211> LENGTH: 1244

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 25

```

agagatgggg acggaggcca cagagcaggt ttcctggggc cattaactctg      50
gggatgaaga ggacgcatac tcggctgagc cactgocgga gctttgctac      100
aaggccgatg tccaggcctt cagccggggc ttccaaccca gtgtctccct      150
gaccctggct gcgctgggtc tggccggcaa tggcctggtc ctggccaccc      200
acctggcagc ccgacgcgca gcgcgctcgc ccacctctgc ccacctgctc      250
cagctggccc tggccgacct cttgctggcc ctgactctgc ccttcgeggc      300
agcaggggct cttcaggget ggagctctgg aagtgccacc tgccgcacca      350
tctctggcct ctactcggcc tccttccacg ccggcttccct cttcctggcc      400
tgtatcagcg ccgaccgcta cgtggccatc gcgcgagcgc tcccagccgg      450
gccgcggccc tccactcccg gccgcgcaca cttggtctcc gtcacgctgt      500
ggctgctgtc actgctcctg gcgctgctg cgctgctctt cagccaggat      550
gggcagcggg aaggccaacg acgctgtcgc ctcactctcc ccgagggcct      600
cacgcagaag gtgaaggggg cgagcgccgt ggcgcaggtg gccctgggct      650
tcgcgctgcc gctgggctgc atggtagcct gctacgcgct tctgggcccgc      700
acgctgctgg ccgccagggg gcccgagcgc cggcgtgcgc tgccgctcgt      750
ggtggtctct gtggcgccct tcgtggtgct gcagctgccc tacagcctcg      800
ccctgctgct ggatactgcc gatctactgg ctgcgcgcga gcggagctgc      850
cctgccagca aacgcaagga tgcgcactg ctggtgacca gcggccttggc      900
cctcgcccgc tgtggcctca atcccgttct ctacgccttc ctgggcctgc      950
gcttccgcca ggacctgagg aggctgctac ggggtgggag ctcgccctca     1000
gggectcaac cccgcgcgcg ctgccccccg cggccccccc tttcttctcg     1050
ctcagctccc acggagaccc acagctctct ctgggacaac tagggctgcg     1100
aatctagagg agggggcagg ctgagggctg tgggaaaggg gtagtagtgg     1150
gggaacactg agaaagaggc agggacctaa agggactacc tctgtgcctt     1200
gccacattaa attgataaca tggaaatgaa aaaaaaaaaa aaaa           1244

```

<210> SEQ ID NO 26

<211> LENGTH: 362

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 26

Met	Gly	Thr	Glu	Ala	Thr	Glu	Gln	Val	Ser	Trp	Gly	His	Tyr	Ser
1				5					10					15

-continued

```

cctcgggttct atcgattgaa ttcattgaaga cattgacctgc catgcttgga      50
actgggaaat tattttgggt cttcttctta atcccatatc tggacatctg      100
gaacatccat gggaaagaat catgtgatgt acagctttat ataaagagac      150
aatctgaaca ctccatctta gcaggagatc cctttgaact agaatgcctt      200
gtgaaatact gtgctaacag gcctcatgtg acttggtgca agctcaatgg      250
aacaacatgt gtaaaacttg aagatagaca aacaagttgg aaggaagaga      300
agaacatttc atttttcatt ctacattttg aaccagtgtc tcctaatagac      350
aatgggtcat accgctgttc tgcaaatTTT cagtctaate tcattgaaag      400
ccactcaaca actctttatg tgacagatgt aaaaagtgtc tcagaacgac      450
cctccaagga cgaaatggca agcagaccct ggctcctgta tagtttactt      500
cctttggggg gattgcctct actcatcaact acctgtttct gcctgttctg      550
ctgcctgaga aggcaccaag gaaagcaaaa tgaactctct gacacagcag      600
gaagggaaat taacctgggt gatgctcacc ttaagagtga gcaaacagaa      650
gcaagcacca ggcaaaattc ccaagtactg ctatcagaaa ctggaattta      700
tgataatgac cctgaccttt gtttcagaat gcaggaaggg tctgaagttt      750
attctaatec atgctgggaa gaaaacaaac caggcattgt ttatgcttcc      800
ctgaaccatt ctgtcattgg actgaactca agactggcaa gaaatgtaa      850
agaagcacca acagaatatg catccatag tgtgaggagt taaggatcct      900
ctagagtoga cctgcagaag cttggccgcc atggcccaac ttgtttattg      950
cagcttataa gtgttacaaa taacaaata atatttctca atttgagaat     1000
ttttacttta gaaatgttca tgttagtgct tgggtctgaa gggtcocatag     1050
gacaaatgat taaaat                                           1066

```

<210> SEQ ID NO 28

<211> LENGTH: 289

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 28

```

Met Lys Thr Leu Pro Ala Met Leu Gly Thr Gly Lys Leu Phe Trp
  1          5          10          15
Val Phe Phe Leu Ile Pro Tyr Leu Asp Ile Trp Asn Ile His Gly
          20          25          30
Lys Glu Ser Cys Asp Val Gln Leu Tyr Ile Lys Arg Gln Ser Glu
          35          40          45
His Ser Ile Leu Ala Gly Asp Pro Phe Glu Leu Glu Cys Pro Val
          50          55          60
Lys Tyr Cys Ala Asn Arg Pro His Val Thr Trp Cys Lys Leu Asn
          65          70          75
Gly Thr Thr Cys Val Lys Leu Glu Asp Arg Gln Thr Ser Trp Lys
          80          85          90
Glu Glu Lys Asn Ile Ser Phe Phe Ile Leu His Phe Glu Pro Val
          95          100          105
Leu Pro Asn Asp Asn Gly Ser Tyr Arg Cys Ser Ala Asn Phe Gln
          110          115          120
Ser Asn Leu Ile Glu Ser His Ser Thr Thr Leu Tyr Val Thr Asp
          125          130          135

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Val Lys Ser Ala Ser Glu Arg Pro Ser Lys Asp Glu Met Ala Ser
 140 145 150
 Arg Pro Trp Leu Leu Tyr Ser Leu Leu Pro Leu Gly Gly Leu Pro
 155 160 165
 Leu Leu Ile Thr Thr Cys Phe Cys Leu Phe Cys Cys Leu Arg Arg
 170 175 180
 His Gln Gly Lys Gln Asn Glu Leu Ser Asp Thr Ala Gly Arg Glu
 185 190 195
 Ile Asn Leu Val Asp Ala His Leu Lys Ser Glu Gln Thr Glu Ala
 200 205 210
 Ser Thr Arg Gln Asn Ser Gln Val Leu Leu Ser Glu Thr Gly Ile
 215 220 225
 Tyr Asp Asn Asp Pro Asp Leu Cys Phe Arg Met Gln Glu Gly Ser
 230 235 240
 Glu Val Tyr Ser Asn Pro Cys Leu Glu Glu Asn Lys Pro Gly Ile
 245 250 255
 Val Tyr Ala Ser Leu Asn His Ser Val Ile Gly Leu Asn Ser Arg
 260 265 270
 Leu Ala Arg Asn Val Lys Glu Ala Pro Thr Glu Tyr Ala Ser Ile
 275 280 285
 Cys Val Arg Ser

<210> SEQ ID NO 29

<211> LENGTH: 2185

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

```

gtttctccttt ccgagccaaa atcccaggcg atggtgaatt atgaacgtgc      50
cacaccatga agctcttggtg gcaggtaact gtgcaccacc acacctggaa      100
tgccatcctg ctcccgttcg tctacctcac ggcgcaagtg tggattctgt      150
gtgcagccat cgctgctgcc gctcagccg ggccccagaa ctgccccctc      200
gtttgctcgt gcagtaacca gttcagcaag gtggtgtgca cggcgccgggg      250
cctctccgag gtcccgcagg gtattccctc gaacaccggt tacctcaacc      300
tcatggagaa caacatccag atgatccagg cggacacctt ccgccacctc      350
caccacctgg aggtcctgca gttgggcagg aactccatcc ggcagattga      400
ggtgggggcc ttcaacggcc tggccagcct caacaccctg gagctgttcg      450
acaactggct gacagtcac cctagcgggg cctttgaata cctgtccaag      500
ctgcccggagc tctggcttcg caacaacccc atcgaaagca tcccccttta      550
cgccctcaac cgggtgccct cctcatgctg cctggacttg ggggagctca      600
agaagctgga gtatatctct gagggagctt ttgaggggct gttcaacctc      650
aagtatctga acttgggcat gtgcaacatt aaagacatgc ccaatctcac      700
ccccctggtg gggctggagg agctggagat gtcagggaac cacttccctg      750
agatcaggcc tggctccttc catggcctga gctccctcaa gaagctctgg      800
gtcatgaact cacaggtcag cctgattgag cggaatgctt ttgacgggct      850
ggcttcaact gtggaactca acttggocca caataacctc tcttctttgc      900
cccatgaact ctttaccocg ctgaggtaac tgggtggagtt gcatctacac      950

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cacaaccctt ggaactgtga ttgtgacatt ctgtggctag cctggtggt 1000
tcgagagtat ataccacca attccacctg ctgtggccgc tgteatgctc 1050
ccatgcacat gcgaggccgc tacctcgtgg aggtggacca ggctccttc 1100
cagtgtctcg ccccttcat catggaogca cctcgagacc tcaacatttc 1150
tgagggtcgg atggcagaac ttaagtgtcg gactccccct atgtcctccg 1200
tgaagtggtt gctgccaat gggacagtgc tcagccacgc ctcccgccac 1250
ccaaggatct ctgtcctcaa cgacggcacc ttgaactttt cccacgtgct 1300
gctttcagac actgggggtg acacatgcat ggtgaccaat gttgcaggca 1350
actccaacgc ctggcctac ctcaatgtga gcacggctga gcttaacacc 1400
tccaactaca gcttcttcac cacagtaaca gtggagacca cggagatctc 1450
gcctgaggac acaacgcgaa agtacaagcc tgttctacc acgtccactg 1500
gttaccagcc ggcatatacc acctctacca cgggtgctcat tcagactacc 1550
cgtgtgcccc agcaggtggc agtaccocgc acagacacca ctgacaagat 1600
gcagaccagc ctggatgaag tcatgaagac caccaagatc atcattggct 1650
gctttgtggc agtgactctg ctagnetccg ccatgttgat tgtcttctat 1700
aaacttcgta agcggcacca gcagcggagt acagtcacag ccgcccggac 1750
tgttgagata atccaggtgg acgaagacat cccagcagca acatcccagc 1800
cagcaacagc agctccgtcc ggtgtatcag gtgagggggc agtagtgctg 1850
cccacaattc atgaccatat taactacaac acctacaaac cagcacatgg 1900
ggccccactg acagaaaaca gcttggggaa ctctctgcac cccacagtca 1950
ccactatctc tgaaccttat ataattcaga cccataccaa ggacaaggta 2000
caggaaactc aaatgatgact cccctcccc aaaaaactta taaaatgcaa 2050
tagaatgcac acaaagacag caacttttgt acagagtggg gagagacttt 2100
ttcttgata tgcttatata ttaagtctat gggctgggta aaaaaaacag 2150
attatattaa aatttaaaga caaaaagtca aaaca 2185

```

<210> SEQ ID NO 30

<211> LENGTH: 653

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 30

```

Met Lys Leu Leu Trp Gln Val Thr Val His His His Thr Trp Asn
  1             5             10             15
Ala Ile Leu Leu Pro Phe Val Tyr Leu Thr Ala Gln Val Trp Ile
             20             25             30
Leu Cys Ala Ala Ile Ala Ala Ala Ala Ser Ala Gly Pro Gln Asn
             35             40             45
Cys Pro Ser Val Cys Ser Cys Ser Asn Gln Phe Ser Lys Val Val
             50             55             60
Cys Thr Arg Arg Gly Leu Ser Glu Val Pro Gln Gly Ile Pro Ser
             65             70             75
Asn Thr Arg Tyr Leu Asn Leu Met Glu Asn Asn Ile Gln Met Ile
             80             85             90
Gln Ala Asp Thr Phe Arg His Leu His His Leu Glu Val Leu Gln
             95             100            105

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Leu	Gly	Arg	Asn	Ser	Ile	Arg	Gln	Ile	Glu	Val	Gly	Ala	Phe	Asn	
				110					115					120	
Gly	Leu	Ala	Ser	Leu	Asn	Thr	Leu	Glu	Leu	Phe	Asp	Asn	Trp	Leu	
				125					130					135	
Thr	Val	Ile	Pro	Ser	Gly	Ala	Phe	Glu	Tyr	Leu	Ser	Lys	Leu	Arg	
				140					145					150	
Glu	Leu	Trp	Leu	Arg	Asn	Asn	Pro	Ile	Glu	Ser	Ile	Pro	Ser	Tyr	
				155					160					165	
Ala	Phe	Asn	Arg	Val	Pro	Ser	Leu	Met	Arg	Leu	Asp	Leu	Gly	Glu	
				170					175					180	
Leu	Lys	Lys	Leu	Glu	Tyr	Ile	Ser	Glu	Gly	Ala	Phe	Glu	Gly	Leu	
				185					190					195	
Phe	Asn	Leu	Lys	Tyr	Leu	Asn	Leu	Gly	Met	Cys	Asn	Ile	Lys	Asp	
				200					205					210	
Met	Pro	Asn	Leu	Thr	Pro	Leu	Val	Gly	Leu	Glu	Glu	Leu	Glu	Met	
				215					220					225	
Ser	Gly	Asn	His	Phe	Pro	Glu	Ile	Arg	Pro	Gly	Ser	Phe	His	Gly	
				230					235					240	
Leu	Ser	Ser	Leu	Lys	Lys	Leu	Trp	Val	Met	Asn	Ser	Gln	Val	Ser	
				245					250					255	
Leu	Ile	Glu	Arg	Asn	Ala	Phe	Asp	Gly	Leu	Ala	Ser	Leu	Val	Glu	
				260					265					270	
Leu	Asn	Leu	Ala	His	Asn	Asn	Leu	Ser	Ser	Leu	Pro	His	Asp	Leu	
				275					280					285	
Phe	Thr	Pro	Leu	Arg	Tyr	Leu	Val	Glu	Leu	His	Leu	His	His	Asn	
				290					295					300	
Pro	Trp	Asn	Cys	Asp	Cys	Asp	Ile	Leu	Trp	Leu	Ala	Trp	Trp	Leu	
				305					310					315	
Arg	Glu	Tyr	Ile	Pro	Thr	Asn	Ser	Thr	Cys	Cys	Gly	Arg	Cys	His	
				320					325					330	
Ala	Pro	Met	His	Met	Arg	Gly	Arg	Tyr	Leu	Val	Glu	Val	Asp	Gln	
				335					340					345	
Ala	Ser	Phe	Gln	Cys	Ser	Ala	Pro	Phe	Ile	Met	Asp	Ala	Pro	Arg	
				350					355					360	
Asp	Leu	Asn	Ile	Ser	Glu	Gly	Arg	Met	Ala	Glu	Leu	Lys	Cys	Arg	
				365					370					375	
Thr	Pro	Pro	Met	Ser	Ser	Val	Lys	Trp	Leu	Leu	Pro	Asn	Gly	Thr	
				380					385					390	
Val	Leu	Ser	His	Ala	Ser	Arg	His	Pro	Arg	Ile	Ser	Val	Leu	Asn	
				395					400					405	
Asp	Gly	Thr	Leu	Asn	Phe	Ser	His	Val	Leu	Leu	Ser	Asp	Thr	Gly	
				410					415					420	
Val	Tyr	Thr	Cys	Met	Val	Thr	Asn	Val	Ala	Gly	Asn	Ser	Asn	Ala	
				425					430					435	
Ser	Ala	Tyr	Leu	Asn	Val	Ser	Thr	Ala	Glu	Leu	Asn	Thr	Ser	Asn	
				440					445					450	
Tyr	Ser	Phe	Phe	Thr	Thr	Val	Thr	Val	Glu	Thr	Thr	Glu	Ile	Ser	
				455					460					465	
Pro	Glu	Asp	Thr	Thr	Arg	Lys	Tyr	Lys	Pro	Val	Pro	Thr	Thr	Ser	
				470					475					480	
Thr	Gly	Tyr	Gln	Pro	Ala	Tyr	Thr	Thr	Ser	Thr	Thr	Val	Leu	Ile	
				485					490					495	
Gln	Thr	Thr	Arg	Val	Pro	Lys	Gln	Val	Ala	Val	Pro	Ala	Thr	Asp	

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	500		505		510
Thr Thr Asp Lys Met Gln Thr Ser Leu Asp Glu Val Met Lys Thr					
	515		520		525
Thr Lys Ile Ile Ile Gly Cys Phe Val Ala Val Thr Leu Leu Ala					
	530		535		540
Ala Ala Met Leu Ile Val Phe Tyr Lys Leu Arg Lys Arg His Gln					
	545		550		555
Gln Arg Ser Thr Val Thr Ala Ala Arg Thr Val Glu Ile Ile Gln					
	560		565		570
Val Asp Glu Asp Ile Pro Ala Ala Thr Ser Ala Ala Ala Thr Ala					
	575		580		585
Ala Pro Ser Gly Val Ser Gly Glu Gly Ala Val Val Leu Pro Thr					
	590		595		600
Ile His Asp His Ile Asn Tyr Asn Thr Tyr Lys Pro Ala His Gly					
	605		610		615
Ala His Trp Thr Glu Asn Ser Leu Gly Asn Ser Leu His Pro Thr					
	620		625		630
Val Thr Thr Ile Ser Glu Pro Tyr Ile Ile Gln Thr His Thr Lys					
	635		640		645
Asp Lys Val Gln Glu Thr Gln Ile					
	650				

<210> SEQ ID NO 31
 <211> LENGTH: 1488
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 31

gctgaaaggg ccacgtttgt ttccattaca aataagacca ccgagtgggc	50
tcttgccgtg gggcggggag cagccgcgcg cagtcttcag aggcagcccc	100
ccaggctgtc tctggagggt gtgtctctgc ttcctttcc ccgtgtttat	150
tttcagacga agccaagtgg cccgggggga cctccggac tcccagcctt	200
cagagaggag ggcagctcgg gctttcgccg cagtgttcc tgcccgtcac	250
gtgtgtgtct ctagccgggg tcgggggagc tggtatcttg gcccttctgg	300
gaggacgcgc acagcccag gaggcagagc cccagacggg aatgggcttt	350
tcagaggtgg ggtgcgggcg aggggacgat gcattatatt taatatttga	400
tttatttttc caactggact tcttcccggg gctctttctg ggcccagctg	450
cctttgtgat cccgcgcccc ggtcctcggc ctctcacctc cagcgcgggg	500
gcgccccctg ctgtcggaaag cggctgtgac cgggcagagg tgctatctgg	550
gactctgggt tctcagcccg gggacagcga accgaggggc agatgatcca	600
tcagaaaaga gccggcactg cccagccccg cgcctctgcc cctgcttttt	650
tccgggagcg cgcgcgcccg caccgcctac ggccgcttga ccccatcttt	700
gagccccgcc ccaagctctg ggaccgtcgt gccctcatc aaggaagagc	750
caaggacccc aaggagaagg tcaggagcgg cgggtgtggat gtcccttggc	800
tgcaggcccc gccgcgcaact ccttcagtc cttcccttct ctagggacca	850
ggtagcatca gtgectggat ctggccttg tgtgcctgc tccctgcccc	900
acctactaag aaccaagtct ggttcaccgg ctcccagag ctggaaccca	950
ttctcagcta gctgggggccc caggccaccc cttccctcca gacctgtgtg	1000

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ccttctgccc tggtccagg gccccccaca ccgtgaccag ggaggatcc      1050
ctatggggct ggccagtcgg caccgtgcca ggcccacagt gccctgggag      1100
tccatggaag tcgttctgtg tctttaaata cagaaggaag acattaacct      1150
ttaggctgaa gaaaatgttt tagtacacag caataactta tttgtcttta      1200
tccaacagcc ataaaatata actttaaata ttctattgat agagaaagga      1250
gttcatgaag gcagaaatgc ctggggccca cgaacatccc agtgtggccc      1300
tggacgggac atcatgctgg gcaacacagc taaaatgagg gtgaagacca      1350
gatttcttgc acatggcggg gacgggatgc tccctagaga gcttcaagtg      1400
gattcttctg tttttatctt ctctcttaat aaaaatgtat gatgtttaca      1450
ttgtcagaga acaaacagaa aaaaaaaaaa aaaaaaaaaa      1488

```

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<210> SEQ ID NO 32
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

```

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<400> SEQUENCE: 32

```

```

Met Ser Leu Gly Cys Arg Pro Arg Arg Ala Leu Pro Ser Val Leu
  1           5           10           15
Pro Phe Ser Arg Asp Gln Val Ala Ser Val Pro Gly Ser Arg Pro
          20           25           30
Cys Val Pro Cys Ser Leu Pro His Leu Leu Arg Thr Lys Ser Gly
          35           40           45
Ser Pro Ala Pro Lys Ser Trp Asn Pro Phe Ser Ala Ser Trp Gly
          50           55           60
Pro Arg Pro Pro Leu Pro Ser Arg Pro Val Cys Leu Leu Pro Trp
          65           70           75
Leu Gln Gly Pro Pro His Arg Asp Gln Gly Gly Ile Pro Met Gly
          80           85           90
Leu Ala Ser Arg His Arg Ala Arg Pro Thr Val Pro Trp Ala Ser
          95           100          105
Met Glu Val Val Leu Cys Leu
          110

```

```

<210> SEQ ID NO 33
<211> LENGTH: 1322
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 33

```

```

atatatcgat atgctgccga ggetgttgct gttgatctgt gctccactct      50
gtgaacctgc cgagctgttt ttgatagcca gccctccca tcccacagag      100
gggagcccag tgaccctgac gtgtaagatg cctttctac agagtccaga      150
tgcccagttc cagttctgct ttttcagaga caccggggcc ttgggcccag      200
gctggagcag ctcccccaag ctccagatcg ctgccatgtg gaaagaagac      250
acagggtcat actggtgcga ggcacagaca atggcgcca aagtcttgag      300
gagcaggaga tcccagataa atgtgcacag ggtccctgtc gctgatgtga      350
gcttgagac tcagccccca ggaggacagg tgatggaggg agacaggctg      400
gtcctcatct gctcagttgc tatgggcaca ggagacatca ccttctttg      450

```

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```

gtacaaaggg gctgtaggtt taaaccttca gtcaaagacc cagcgttcac      500
tgacagcaga gtatgagatt ccttcagtga gggagagtga tgctgagcaa      550
tattactgtg tagctgaaaa tggctatggt cccagcccca gtgggctggt      600
gagcatcact gtcagaatcc cgggtgtctcg cccaatcctc atgctcaggg      650
ctcccagggc ccaggctgca gtggaggatg tgctggagct tcaactgtgag      700
gccctgagag gctctctccc gatcctgtac tggttttatc acgaggatat      750
caccttgggg agcaggtcgg cccctctctg aggaggagcc tccttcaacc      800
tttcctgac  tgaagaacat tctggaact  actcctgtga ggccaacaat      850
ggcctggggg cccagcgcag tgaggcggtg acaactcaact tcacagtgcc      900
tactggggcc agaagcaatc atcttaoctc aggagtcatt gaggggctgc      950
tcagcacctc tggccagacc accgtggcct tattattttg ctacggcctc     1000
aaaagaaaaa taggaagacg ttcagccagg gatccactca ggagccttcc     1050
cagccctcta cccaagagt  tcacgtacct caactcacct accccagggc     1100
agctacagcc tataatgaa  aatgtgaatg ttgtaagtg  ggatgaggtt     1150
tattcaactg cgtactataa  ccagccggag caggaatcag tagcagcaga     1200
aaccttgggg acacatatgg  aggacaaggt ttccttagac atctattcca     1250
ggctgaggaa agcaaacatt  acagatgtgg actatgaaga tgctatgtaa     1300
ggttatggaa gattctgctc  tt                                     1322

```

<210> SEQ ID NO 34

<211> LENGTH: 429

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 34

```

Met Leu Pro Arg Leu Leu Leu Ile Cys Ala Pro Leu Cys Glu
 1          5          10          15
Pro Ala Glu Leu Phe Leu Ile Ala Ser Pro Ser His Pro Thr Glu
          20          25          30
Gly Ser Pro Val Thr Leu Thr Cys Lys Met Pro Phe Leu Gln Ser
          35          40          45
Ser Asp Ala Gln Phe Gln Phe Cys Phe Phe Arg Asp Thr Arg Ala
          50          55          60
Leu Gly Pro Gly Trp Ser Ser Ser Pro Lys Leu Gln Ile Ala Ala
          65          70          75
Met Trp Lys Glu Asp Thr Gly Ser Tyr Trp Cys Glu Ala Gln Thr
          80          85          90
Met Ala Ser Lys Val Leu Arg Ser Arg Arg Ser Gln Ile Asn Val
          95          100          105
His Arg Val Pro Val Ala Asp Val Ser Leu Glu Thr Gln Pro Pro
          110          115          120
Gly Gly Gln Val Met Glu Gly Asp Arg Leu Val Leu Ile Cys Ser
          125          130          135
Val Ala Met Gly Thr Gly Asp Ile Thr Phe Leu Trp Tyr Lys Gly
          140          145          150
Ala Val Gly Leu Asn Leu Gln Ser Lys Thr Gln Arg Ser Leu Thr
          155          160          165
Ala Glu Tyr Glu Ile Pro Ser Val Arg Glu Ser Asp Ala Glu Gln
          170          175          180

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Tyr Tyr Cys Val Ala Glu Asn Gly Tyr Gly Pro Ser Pro Ser Gly
 185 190 195
 Leu Val Ser Ile Thr Val Arg Ile Pro Val Ser Arg Pro Ile Leu
 200 205 210
 Met Leu Arg Ala Pro Arg Ala Gln Ala Ala Val Glu Asp Val Leu
 215 220 225
 Glu Leu His Cys Glu Ala Leu Arg Gly Ser Pro Pro Ile Leu Tyr
 230 235 240
 Trp Phe Tyr His Glu Asp Ile Thr Leu Gly Ser Arg Ser Ala Pro
 245 250 255
 Ser Gly Gly Gly Ala Ser Phe Asn Leu Ser Leu Thr Glu Glu His
 260 265 270
 Ser Gly Asn Tyr Ser Cys Glu Ala Asn Asn Gly Leu Gly Ala Gln
 275 280 285
 Arg Ser Glu Ala Val Thr Leu Asn Phe Thr Val Pro Thr Gly Ala
 290 295 300
 Arg Ser Asn His Leu Thr Ser Gly Val Ile Glu Gly Leu Leu Ser
 305 310 315
 Thr Leu Gly Pro Ala Thr Val Ala Leu Leu Phe Cys Tyr Gly Leu
 320 325 330
 Lys Arg Lys Ile Gly Arg Arg Ser Ala Arg Asp Pro Leu Arg Ser
 335 340 345
 Leu Pro Ser Pro Leu Pro Gln Glu Phe Thr Tyr Leu Asn Ser Pro
 350 355 360
 Thr Pro Gly Gln Leu Gln Pro Ile Tyr Glu Asn Val Asn Val Val
 365 370 375
 Ser Gly Asp Glu Val Tyr Ser Leu Ala Tyr Tyr Asn Gln Pro Glu
 380 385 390
 Gln Glu Ser Val Ala Ala Glu Thr Leu Gly Thr His Met Glu Asp
 395 400 405
 Lys Val Ser Leu Asp Ile Tyr Ser Arg Leu Arg Lys Ala Asn Ile
 410 415 420
 Thr Asp Val Asp Tyr Glu Asp Ala Met
 425

<210> SEQ ID NO 35

<211> LENGTH: 685

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 35

gatgtgctcc ttggagctgg tgtgcagtgt cctgactgta agatcaagtc 50
 caaacctggt ttggaattga ggaaacttct cttttgatct cagcccttgg 100
 tgggtccaggt cttcatgctg ctgtgggtga tattactggg cctggctcct 150
 gtcagtggac agtttgcaag gacaccagc cccattatct tcctccagcc 200
 tccatggacc acagtcttcc aaggagagag agtgaccctc acttgcaagg 250
 gatttcgctt ctactacca cagaaaacaa aatggtacca tcggtacctt 300
 gggaaagaaa tactaagaga aaccccagac aatctccttg aggttcagga 350
 atctggagag tacagatgcc aggccaggg ctcccccttc agtagccctg 400
 tgcacttggg tttttcttca gagatgggat ttctctatgc tgcccaggct 450
 aatgttgaac tcctgggctc aagtgatctg ctcacctagg cctctcaaag 500

-continued

```

cgctgggatt acagcttgcg tgatcctgca agctccactt tctgtgtttg      550
aaggagactc tgtggttctg agtgccggg caaaggcggg agtaacactg      600
aataatacta tttacaagaa tgataatgtc ctggcattcc ttaataaaag      650
aactgacttc caaaaaaaaa aaaaaaaaaa aaaaaa                      685

```

```

<210> SEQ ID NO 36
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 36

```

```

Met Leu Leu Trp Val Ile Leu Leu Val Leu Ala Pro Val Ser Gly
  1           5           10           15
Gln Phe Ala Arg Thr Pro Arg Pro Ile Ile Phe Leu Gln Pro Pro
          20           25           30
Trp Thr Thr Val Phe Gln Gly Glu Arg Val Thr Leu Thr Cys Lys
          35           40           45
Gly Phe Arg Phe Tyr Ser Pro Gln Lys Thr Lys Trp Tyr His Arg
          50           55           60
Tyr Leu Gly Lys Glu Ile Leu Arg Glu Thr Pro Asp Asn Ile Leu
          65           70           75
Glu Val Gln Glu Ser Gly Glu Tyr Arg Cys Gln Ala Gln Gly Ser
          80           85           90
Pro Leu Ser Ser Pro Val His Leu Asp Phe Ser Ser Glu Met Gly
          95          100          105
Phe Pro His Ala Ala Gln Ala Asn Val Glu Leu Leu Gly Ser Ser
          110          115          120
Asp Leu Leu Thr

```

```

<210> SEQ ID NO 37
<211> LENGTH: 1337
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 37

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```

ggatttttgt gatccgcgat tcgctccac gggcgggacc tttgtaactg      50
egggaggccc aggacaggcc caccctgccc ggcgggaggc agccgggggtg      100
agggagggtga agaaaccaag acgcagagag gccaaagcccc ttgccttggg      150
tcacacagcc aaaggaggca gagccagaac tcacaaccag atccagaggc      200
aacagggaca tggccacctg ggacgaaaag gcagtcaccc gcaggggccaa      250
ggtggctccc gctgagagga tgagcaagtt ctttaaggcac ttcacggctc      300
tgggagacga ctaccatgcc tggaaatca actacaagaa atgggagaat      350
gaagaggagg aggaggagga ggagcagcca ccaccacac cagtctcagg      400
cgaggaaggc agagctgcag cccctgacgt tgcccctgcc cctggccccg      450
caccagggc cccccttgac ttcaggggca tgttgaggaa actgttcagc      500
tcccacaggt ttcaggtcat catcatctgc ttggtggttc tggatgccct      550
cctggtgctt gctgagctca tcctggacct gaagatcacc cagcccgaca      600
agaataacta tgctgccatg gtattccact acatgagcat caccatcttg      650
gtctttttta tgatggagat catctttaa ttattgtct tccgcctgag      700

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ttctttcacc acaagtttga gatcctggat gcccgctgctg gtggtggtct      750
cattcatcct ggacattgtc ctctctgttc aggagcacca gtttgaggct      800
ctgggcctgc tgattctgct cgggtgtgg cgggtggccc ggatcatcaa      850
tgggattatc atctcagtta agacacgttc agaacggcaa ctcttaaggt      900
taaaacagat gaatgtacaa ttggccgcca agattcaaca ccttgagttc      950
agctgctctg agaagcccct ggactgatga gtttgctgta tcaacctgta     1000
aggagaagct ctctccggat ggctatggga atgaaagaat ccgacttcta     1050
ctctcacaca gccaccgtga aagtcttggg gtaaaatgtg ctgtgtacag     1100
aagagagaga aggaagcagg ctggcatgtt cactgggctg gtgttacgac     1150
agagaacctg acagtcaactg gccagttatc acttcagatt acaaatcaca     1200
cagagcatct gcctgttttc aatcacaaga gaacaaaacc aaaatctata     1250
aagatattct gaaaatatga cagaatttga caaataaaag cataaacgtg     1300
taaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa      1337

```

<210> SEQ ID NO 38

<211> LENGTH: 255

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 38

```

Met Ala Thr Trp Asp Glu Lys Ala Val Thr Arg Arg Ala Lys Val
  1          5          10         15
Ala Pro Ala Glu Arg Met Ser Lys Phe Leu Arg His Phe Thr Val
          20          25          30
Val Gly Asp Asp Tyr His Ala Trp Asn Ile Asn Tyr Lys Lys Trp
          35          40          45
Glu Asn Glu Glu Glu Glu Glu Glu Glu Gln Pro Pro Pro Thr
          50          55          60
Pro Val Ser Gly Glu Glu Gly Arg Ala Ala Ala Pro Asp Val Ala
          65          70          75
Pro Ala Pro Gly Pro Ala Pro Arg Ala Pro Leu Asp Phe Arg Gly
          80          85          90
Met Leu Arg Lys Leu Phe Ser Ser His Arg Phe Gln Val Ile Ile
          95          100         105
Ile Cys Leu Val Val Leu Asp Ala Leu Leu Val Leu Ala Glu Leu
          110         115         120
Ile Leu Asp Leu Lys Ile Ile Gln Pro Asp Lys Asn Asn Tyr Ala
          125         130         135
Ala Met Val Phe His Tyr Met Ser Ile Thr Ile Leu Val Phe Phe
          140         145         150
Met Met Glu Ile Ile Phe Lys Leu Phe Val Phe Arg Leu Ser Ser
          155         160         165
Phe Thr Thr Ser Leu Arg Ser Trp Met Pro Val Val Val Val Val
          170         175         180
Ser Phe Ile Leu Asp Ile Val Leu Leu Phe Gln Glu His Gln Phe
          185         190         195
Glu Ala Leu Gly Leu Leu Ile Leu Leu Arg Leu Trp Arg Val Ala
          200         205         210
Arg Ile Ile Asn Gly Ile Ile Ile Ser Val Lys Thr Arg Ser Glu
          215         220         225

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Arg Gln Leu Leu Arg Leu Lys Gln Met Asn Val Gln Leu Ala Ala
230 235 240

Lys Ile Gln His Leu Glu Phe Ser Cys Ser Glu Lys Pro Leu Asp
245 250 255

<210> SEQ ID NO 39

<211> LENGTH: 2970

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 39

```

agtgaagggg tttcccatat gaaaaataca gaaagaatta tttgaatact      50
agcaaatata caacttgata tttctagaga acccaggcac agtcttgagg      100
acattactoc tgagagactg cagctgatgg aagatgagcc ccaacttcta      150
aaaatgtatc actaccggga ttgagataca aacagcattt aggaaggctc      200
catctgagta gcagcttctc gccctccttc ttggagataa gtcgggcttt      250
tggtgagaca gactttccca accctctgcc cggccgggtgc ccatgcttct      300
gtggctgctg ctgctgatcc tgactcctgg aagagaacaa tcaggggtgg      350
ccccaaaagc tgtacttctc ctcaatctc catggtccac agccttcaaa      400
ggagaaaaag tggctctcat atgcagcagc atatcacatt ccctagccca      450
gggagacaca tattggtatc acgatgagaa gttgttgaaa ataaaacatg      500
acaagatcca aattacagag cctggaaatt accaatgtaa gaccggagga      550
tcctccctca gtgatgcctg gcatgtgaa ttttcacctg actggctgat      600
cctgcaggct ttacatcctg tctttgaagg agacaatgtc attctgagat      650
gtcaggggaa agacaacaaa aacactcctc aaaagggtta ctacaaggat      700
ggaaaacagc tcctaataag ttataattta gagaagatca cagtgaattc      750
agtctccagg gataatagca aatatcattg tactgcttat aggaagtttt      800
acatacttga cattgaagta acttcaaac ccctaaatat ccaagttcaa      850
gagctgtttc tacatcctgt gctgagagcc agctcttcca cgccataga      900
ggggagtccc atgacctga cctgtgagac ccagctctct ccacagaggc      950
cagatgtcca gctgcaattc tcctcttca gagatagcca gacctcgga      1000
ttgggctgga gcaggctccc cagactccag atccctgcca tgtggactga      1050
agactcaggg tcttactggt gtgaggtgga gacagtgact cacagcatca      1100
aaaaaaggag cctgagatct cagatacgtg tacagagagt ccctgtgtct      1150
aatgtgaatc tagagatccg gccaccgga gggcagctga ttgaaggaga      1200
aaatatggtc cttatttctc cagtagccca ggggtcaggg actgtcacat      1250
tctctggcca caaagaagga agagtaagaa gcctgggtag aaagaccag      1300
cgttccctgt tggcagagct gcatgttctc accgtgaagg agagtgatgc      1350
agggagatag tactgtgcag ctgataacgt tcacagcccc atcctcagca      1400
cgtggattcg agtcaccgtg agaattccgg tatctcacc tgtectcacc      1450
ttcagggctc ccagggccca cactgtggtg ggggacctgc tggagcttca      1500
ctgtgagtcc ctgagaggct cteccccgat cctgtaccga ttttateatg      1550
aggatgtcac cctggggaac agctcagccc cctctggagg aggagcctcc      1600
ttcaacctct ctctgactgc agaacattct ggaaactact cctgtgatgc      1650

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agacaatggc ctgggggccc agcacagtca tggagtgagt ctcagggtca      1700
cagttccggg gtctcgcccc gtcctcacc ctagggtccc cggggcccag      1750
gctgtggtgg gggacctgct ggagcttcac tgtgagtcct tgagaggctc      1800
cttcccgatc ctgtactggt tttatcacga ggatgacacc ttggggaaca      1850
tctcgcccca ctctggagga ggggcatcct tcaacctctc tctgactaca      1900
gaacattctg gaaactactc atgtgaggct gacaatggcc tgggggcccc      1950
gcacagtaaa gtggtgacac tcaatgttac aggaacttcc aggaacagaa      2000
caggccttac cgctgcggga atcacggggc tgggtctcag catcctcgtc      2050
cttgctgctg ctgctgctct gctgcattac gccaggggccc gaaggaaacc      2100
aggaggactt tctgccactg gaacatctag tcacagtctc agtgagtgtc      2150
aggagccttc ctgctccagg ccttcagga tagacctca agagcccact      2200
cactctaaac cactagcccc aatggagctg gagccaatgt acagcaatgt      2250
aaatcctgga gatagcaacc cgatttattc ccagatctgg agcatccagc      2300
atacaaaaaga aaactcagct aattgtccaa tgatgcatca agagcatgag      2350
gaacttacag tcctctattc agaactgaag aagacacacc cagacgactc      2400
tgcaggggag gctagcagca gaggcagggc ccatgaagaa gatgatgaag      2450
aaaactatga gaatgtacca cgtgtattac tggcctcaga cactagccc      2500
cttaccaga gtggcccaca gaaacagcc tgcaccattt tttttctgt      2550
tctctccaac cacacatcat ccatctctcc agactctgcc tcctacgagg      2600
ctgggctgca gggtatgtga ggctgagcaa aaggctgca aatctccct      2650
gtgctgatac tgtgtgttcc ccaggaagag agcaggcagc ctctgagcaa      2700
gcactgtggt attttcacag tggagacacg tggcaaggca ggagggccct      2750
cagctcctag ggctgtcgaa tagaggagga gagagaaatg gtctagccag      2800
ggttacaagg gcacaatcat gaccatttga tccaagtgtg atcgaaagct      2850
gttaatgtgc tctctgtata aacaatttgc tccaaatatt ttgtttccct      2900
tttttgtgtg gctggtagtg gcattgctga tgttttggtg tatatgctgt      2950
atccttgcta ccatattggg      2970

```

<210> SEQ ID NO 40

<211> LENGTH: 734

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 40

```

Met Leu Leu Trp Leu Leu Leu Leu Ile Leu Thr Pro Gly Arg Glu
  1             5             10             15

Gln Ser Gly Val Ala Pro Lys Ala Val Leu Leu Leu Asn Pro Pro
          20             25             30

Trp Ser Thr Ala Phe Lys Gly Glu Lys Val Ala Leu Ile Cys Ser
          35             40             45

Ser Ile Ser His Ser Leu Ala Gln Gly Asp Thr Tyr Trp Tyr His
          50             55             60

Asp Glu Lys Leu Leu Lys Ile Lys His Asp Lys Ile Gln Ile Thr
          65             70             75

Glu Pro Gly Asn Tyr Gln Cys Lys Thr Arg Gly Ser Ser Leu Ser

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	80								85					90
Asp	Ala	Val	His	Val	Glu	Phe	Ser	Pro	Asp	Trp	Leu	Ile	Leu	Gln
				95					100					105
Ala	Leu	His	Pro	Val	Phe	Glu	Gly	Asp	Asn	Val	Ile	Leu	Arg	Cys
				110					115					120
Gln	Gly	Lys	Asp	Asn	Lys	Asn	Thr	His	Gln	Lys	Val	Tyr	Tyr	Lys
				125					130					135
Asp	Gly	Lys	Gln	Leu	Pro	Asn	Ser	Tyr	Asn	Leu	Glu	Lys	Ile	Thr
				140					145					150
Val	Asn	Ser	Val	Ser	Arg	Asp	Asn	Ser	Lys	Tyr	His	Cys	Thr	Ala
				155					160					165
Tyr	Arg	Lys	Phe	Tyr	Ile	Leu	Asp	Ile	Glu	Val	Thr	Ser	Lys	Pro
				170					175					180
Leu	Asn	Ile	Gln	Val	Gln	Glu	Leu	Phe	Leu	His	Pro	Val	Leu	Arg
				185					190					195
Ala	Ser	Ser	Ser	Thr	Pro	Ile	Glu	Gly	Ser	Pro	Met	Thr	Leu	Thr
				200					205					210
Cys	Glu	Thr	Gln	Leu	Ser	Pro	Gln	Arg	Pro	Asp	Val	Gln	Leu	Gln
				215					220					225
Phe	Ser	Leu	Phe	Arg	Asp	Ser	Gln	Thr	Leu	Gly	Leu	Gly	Trp	Ser
				230					235					240
Arg	Ser	Pro	Arg	Leu	Gln	Ile	Pro	Ala	Met	Trp	Thr	Glu	Asp	Ser
				245					250					255
Gly	Ser	Tyr	Trp	Cys	Glu	Val	Glu	Thr	Val	Thr	His	Ser	Ile	Lys
				260					265					270
Lys	Arg	Ser	Leu	Arg	Ser	Gln	Ile	Arg	Val	Gln	Arg	Val	Pro	Val
				275					280					285
Ser	Asn	Val	Asn	Leu	Glu	Ile	Arg	Pro	Thr	Gly	Gly	Gln	Leu	Ile
				290					295					300
Glu	Gly	Glu	Asn	Met	Val	Leu	Ile	Cys	Ser	Val	Ala	Gln	Gly	Ser
				305					310					315
Gly	Thr	Val	Thr	Phe	Ser	Trp	His	Lys	Glu	Gly	Arg	Val	Arg	Ser
				320					325					330
Leu	Gly	Arg	Lys	Thr	Gln	Arg	Ser	Leu	Leu	Ala	Glu	Leu	His	Val
				335					340					345
Leu	Thr	Val	Lys	Glu	Ser	Asp	Ala	Gly	Arg	Tyr	Tyr	Cys	Ala	Ala
				350					355					360
Asp	Asn	Val	His	Ser	Pro	Ile	Leu	Ser	Thr	Trp	Ile	Arg	Val	Thr
				365					370					375
Val	Arg	Ile	Pro	Val	Ser	His	Pro	Val	Leu	Thr	Phe	Arg	Ala	Pro
				380					385					390
Arg	Ala	His	Thr	Val	Val	Gly	Asp	Leu	Leu	Glu	Leu	His	Cys	Glu
				395					400					405
Ser	Leu	Arg	Gly	Ser	Pro	Pro	Ile	Leu	Tyr	Arg	Phe	Tyr	His	Glu
				410					415					420
Asp	Val	Thr	Leu	Gly	Asn	Ser	Ser	Ala	Pro	Ser	Gly	Gly	Gly	Ala
				425					430					435
Ser	Phe	Asn	Leu	Ser	Leu	Thr	Ala	Glu	His	Ser	Gly	Asn	Tyr	Ser
				440					445					450
Cys	Asp	Ala	Asp	Asn	Gly	Leu	Gly	Ala	Gln	His	Ser	His	Gly	Val
				455					460					465
Ser	Leu	Arg	Val	Thr	Val	Pro	Val	Ser	Arg	Pro	Val	Leu	Thr	Leu
				470					475					480

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Arg Ala Pro Gly Ala Gln Ala Val Val Gly Asp Leu Leu Glu Leu
 485 490 495
 His Cys Glu Ser Leu Arg Gly Ser Phe Pro Ile Leu Tyr Trp Phe
 500 505 510
 Tyr His Glu Asp Asp Thr Leu Gly Asn Ile Ser Ala His Ser Gly
 515 520 525
 Gly Gly Ala Ser Phe Asn Leu Ser Leu Thr Thr Glu His Ser Gly
 530 535 540
 Asn Tyr Ser Cys Glu Ala Asp Asn Gly Leu Gly Ala Gln His Ser
 545 550 555
 Lys Val Val Thr Leu Asn Val Thr Gly Thr Ser Arg Asn Arg Thr
 560 565 570
 Gly Leu Thr Ala Ala Gly Ile Thr Gly Leu Val Leu Ser Ile Leu
 575 580 585
 Val Leu Ala Ala Ala Ala Ala Leu Leu His Tyr Ala Arg Ala Arg
 590 595 600
 Arg Lys Pro Gly Gly Leu Ser Ala Thr Gly Thr Ser Ser His Ser
 605 610 615
 Pro Ser Glu Cys Gln Glu Pro Ser Ser Ser Arg Pro Ser Arg Ile
 620 625 630
 Asp Pro Gln Glu Pro Thr His Ser Lys Pro Leu Ala Pro Met Glu
 635 640 645
 Leu Glu Pro Met Tyr Ser Asn Val Asn Pro Gly Asp Ser Asn Pro
 650 655 660
 Ile Tyr Ser Gln Ile Trp Ser Ile Gln His Thr Lys Glu Asn Ser
 665 670 675
 Ala Asn Cys Pro Met Met His Gln Glu His Glu Glu Leu Thr Val
 680 685 690
 Leu Tyr Ser Glu Leu Lys Lys Thr His Pro Asp Asp Ser Ala Gly
 695 700 705
 Glu Ala Ser Ser Arg Gly Arg Ala His Glu Glu Asp Asp Glu Glu
 710 715 720
 Asn Tyr Glu Asn Val Pro Arg Val Leu Leu Ala Ser Asp His
 725 730

<210> SEQ ID NO 41

<211> LENGTH: 3459

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 41

```

ctcaatcagc tttatgcaga gaagaagctt actgagctca ctgctggtgc      50
tggtgtaggc aagtgctgct ttggcaatct gggctgacct ggcttgctc      100
ctcagaactc cttctccaac cctggagcag gcttccatgc tgctgtgggc      150
gtccttgctg gcctttgctc cagtctgtgg acaatctgca gctgcacaca      200
aacctgtgat ttccgtccat cctccatgga ccacattctt caaaggagag      250
agagtgactc tgacttgcaa tggatttcag ttctatgcaa cagagaaaac      300
aacatggtat categgcact actggggaga aaagttgacc ctgaccccag      350
gaaacacctc cgaggttcgg gaatctggac tgtacagatg ccaggcccgg      400
ggctccccac gaagtaacce tgtgcgcttg ctcttttctt cagactcctt      450
aatcctgcag gcacatatt ctgtgtttga aggtgacaca ttggttctga      500
  
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gatgccacag aagaaggaaa gagaaattga ctgctgtgaa atatacttgg	550
aatggaaaca ttctttccat ttctaataaa agctgggatc ttcttatccc	600
acaagcaagt tcaataaca atggcaatta tcgatgcatt ggatattggag	650
atgagaatga tgtatttaga tcaaatcca aaataattaa aattcaagaa	700
ctatttcac atccagagct gaaagctaca gactctcagc ctacagaggg	750
gaattctgta aacctgagct gtgaaacaca gcttctcca gagcggtcag	800
acaccccaact tcaactcaac ttcttcagag atggcgagggt catcctgtca	850
gactggagca cgtaccggga actccagctc ccaaccgtct ggagagaaaa	900
ctcaggatcc tattggtgtg gtgctgaaac agtgaggggt aacatccaca	950
agcacagtcc ctgctacag atccatgtgc agcggatccc tgtgtctggg	1000
gtgctcctgg agaccagcc ctacaggggc caggctgttg aaggggagat	1050
gctggtcctt gtctgctccg tggctgaagg cacaggggat accacattct	1100
cctggcaccg agaggacatg caggagagtc tggggaggaa aactcagcgt	1150
tccctgagag cagagctgga gctccctgcc atcagacaga gccatgcagg	1200
gggatactac tgtacagcag acaacagcta cggccctgtc cagagcatgg	1250
tgtggaatgt cactgtgaga gagaccccag gcaacagaga tggccttgtc	1300
gccgcgggag cactggagg gctgctcagt gctcttctcc tggctgtggc	1350
cctgtgttt cactgctggc gtcggaggaa gtcaggagtt ggtttcttgg	1400
gagacgaaac caggctccct ccgctccag gccaggaga gtctcccat	1450
tccatctgcc ctgcccaggt ggagctcag tcgttgatg ttgatgtaca	1500
ccccaaaaag ggagatttgg tatactctga gatccagact actcagctgg	1550
gagaagaaga ggaagctaata acctccagga cactctaga ggataaggat	1600
gtctcagttg tctactctga ggtaaagaca caacaccag ataactcagc	1650
tggaaagatc agctctaagg atgaagaaaag ttaagagaat gaaaagtac	1700
gggaacgtcc tactcatgtg atttctccct tgtccaaagt cccaggccca	1750
gtgcagtcct tgcggcacct ggaatgatca actcattcca gctttctaat	1800
tcttctcatg catatgcatt cactcccagg aatactcatt cgtctactct	1850
gatgttggga tggaatggcc tctgaaagac ttcactaaaa tgaccaggat	1900
ccacagttaa gagaagacc tgtagtattt gctgtgggcc tgacctaatg	1950
cattccctag ggtctgcttt agagaagggg gataaagaga gagaaggact	2000
gttatgaaaa acagaagcac aaatcttggg gaattgggat ttgcagagat	2050
gaaaaagact gggtgacctg gatctctgct taatacatct acaaccattg	2100
tctcactgga gactcacttg catcagtttg tttaactgtg agtggctgca	2150
caggcactgt gcaaaaatg aaaagcccct tcaactctgc ctgcacagct	2200
tacactgtca ggattcagtt gcagattaaa gaaccatctt ggaatggttt	2250
acagagagag gaatttaaaa gaggacatca gaagagctgg agatgcaagc	2300
tctaggctgc gcttccaaaa gcaaatgata attatgtaa tgcatttagt	2350
gacaaagatt tgcaacatta gagaaaagag acacaaatat aaaattaaaa	2400
acttaagtac caactctoca aaactaaatt tgaactaaa atattagtat	2450

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aaactcataa taaactctgc ctttaaaaa agataaatat ttctacgtc      2500
tgttcactga aataattacc aaccoccttag caataagcac tccttgacaga    2550
gaggttttat tctctaaata ccattccctt ctcaaaggaa ataaggttgc    2600
ttttcttgta ggaactgtgt ctttgagtta ctaattagtt tataatgagaa    2650
taattcctgc aataaatgaa gaaggaataa aagaaatagg aagccacaaa    2700
tttgatgga tatttcatga tacacctact ggttaataa ttgacaaaa    2750
ccagcagcca aatattagag gtctcctgat ggaagtgtac aataccacct    2800
acaaattatc catgccccea gtgttaaac tgaatccatt caagtcttc      2850
taactgaata cttgttttat agaaaatgca tggagaaaag gaatttgttt    2900
aaataacatt atgggattgc aaccagcaaa acataaactg agaaaaagtt    2950
ctatagggca aatcacctgg cttctataac aaataaatgg gaaaaaatg     3000
aaataaaaag aagagagggg ggaagaaagg gagagagaag aaaagaaaa    3050
tgaagaaaag taattagaat attttcaaca taaagaaaag acgaatattt    3100
aaggtgacag atatccaac tacgctgatt tgatctttac aaatttatg     3150
agtgtatgaa tttgtcacat gtatcacccc caaaaaaga gaaaagaaa    3200
aatagaagac atataaatta aatgagacga gacatgtcga ccaaaaggaa    3250
tgtgtgggtc ttgtttggat cctgactcaa attaagaaaa aataaaacta    3300
cctacgaaat actaagaaaa atttgtatac taatattaag aaattgttgt    3350
gtgttttggg tataagtgat agtttattgt agtgatgttt ttataaaagc    3400
aaaaggatat tcactttcag cgcttatact gaagtattag attaaagctt    3450
attaacgta      3459

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<210> SEQ ID NO 42

<211> LENGTH: 515

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 42

```

Met Leu Leu Trp Ala Ser Leu Leu Ala Phe Ala Pro Val Cys Gly
 1          5          10          15
Gln Ser Ala Ala Ala His Lys Pro Val Ile Ser Val His Pro Pro
          20          25          30
Trp Thr Thr Phe Phe Lys Gly Glu Arg Val Thr Leu Thr Cys Asn
          35          40          45
Gly Phe Gln Phe Tyr Ala Thr Glu Lys Thr Thr Trp Tyr His Arg
          50          55          60
His Tyr Trp Gly Glu Lys Leu Thr Leu Thr Pro Gly Asn Thr Leu
          65          70          75
Glu Val Arg Glu Ser Gly Leu Tyr Arg Cys Gln Ala Arg Gly Ser
          80          85          90
Pro Arg Ser Asn Pro Val Arg Leu Leu Phe Ser Ser Asp Ser Leu
          95          100          105
Ile Leu Gln Ala Pro Tyr Ser Val Phe Glu Gly Asp Thr Leu Val
          110          115          120
Leu Arg Cys His Arg Arg Arg Lys Glu Lys Leu Thr Ala Val Lys
          125          130          135
Tyr Thr Trp Asn Gly Asn Ile Leu Ser Ile Ser Asn Lys Ser Trp
          140          145          150

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Asp Leu Leu Ile Pro Gln Ala Ser Ser Asn Asn Asn Gly Asn Tyr
 155 160 165
 Arg Cys Ile Gly Tyr Gly Asp Glu Asn Asp Val Phe Arg Ser Asn
 170 175 180
 Phe Lys Ile Ile Lys Ile Gln Glu Leu Phe Pro His Pro Glu Leu
 185 190 195
 Lys Ala Thr Asp Ser Gln Pro Thr Glu Gly Asn Ser Val Asn Leu
 200 205 210
 Ser Cys Glu Thr Gln Leu Pro Pro Glu Arg Ser Asp Thr Pro Leu
 215 220 225
 His Phe Asn Phe Phe Arg Asp Gly Glu Val Ile Leu Ser Asp Trp
 230 235 240
 Ser Thr Tyr Pro Glu Leu Gln Leu Pro Thr Val Trp Arg Glu Asn
 245 250 255
 Ser Gly Ser Tyr Trp Cys Gly Ala Glu Thr Val Arg Gly Asn Ile
 260 265 270
 His Lys His Ser Pro Ser Leu Gln Ile His Val Gln Arg Ile Pro
 275 280 285
 Val Ser Gly Val Leu Leu Glu Thr Gln Pro Ser Gly Gly Gln Ala
 290 295 300
 Val Glu Gly Glu Met Leu Val Leu Val Cys Ser Val Ala Glu Gly
 305 310 315
 Thr Gly Asp Thr Thr Phe Ser Trp His Arg Glu Asp Met Gln Glu
 320 325 330
 Ser Leu Gly Arg Lys Thr Gln Arg Ser Leu Arg Ala Glu Leu Glu
 335 340 345
 Leu Pro Ala Ile Arg Gln Ser His Ala Gly Gly Tyr Tyr Cys Thr
 350 355 360
 Ala Asp Asn Ser Tyr Gly Pro Val Gln Ser Met Val Leu Asn Val
 365 370 375
 Thr Val Arg Glu Thr Pro Gly Asn Arg Asp Gly Leu Val Ala Ala
 380 385 390
 Gly Ala Thr Gly Gly Leu Leu Ser Ala Leu Leu Leu Ala Val Ala
 395 400 405
 Leu Leu Phe His Cys Trp Arg Arg Arg Lys Ser Gly Val Gly Phe
 410 415 420
 Leu Gly Asp Glu Thr Arg Leu Pro Pro Ala Pro Gly Pro Gly Glu
 425 430 435
 Ser Ser His Ser Ile Cys Pro Ala Gln Val Glu Leu Gln Ser Leu
 440 445 450
 Tyr Val Asp Val His Pro Lys Lys Gly Asp Leu Val Tyr Ser Glu
 455 460 465
 Ile Gln Thr Thr Gln Leu Gly Glu Glu Glu Glu Ala Asn Thr Ser
 470 475 480
 Arg Thr Leu Leu Glu Asp Lys Asp Val Ser Val Val Tyr Ser Glu
 485 490 495
 Val Lys Thr Gln His Pro Asp Asn Ser Ala Gly Lys Ile Ser Ser
 500 505 510
 Lys Asp Glu Glu Ser
 515

<210> SEQ ID NO 43

<211> LENGTH: 1933

-continued

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 43

acacacccac aggacctgca gctgaacgaa gttgaagaca actcaggaga	50
tctgttgtaa agagaacgat agaggaaaat atatgaatgt tgccatcttt	100
agttccctgt gttgggaaaa ctgtctggct gtacctccaa gcctggccaa	150
accctgtggt tgaaggagat gcctgactc tgcgatgtca gggatggaag	200
aatacaccac tgtctcaggt gaagttctac agagatggaa aattccttca	250
tttctctaag gaaaaccaga ctctgtccat gggagcagca acagtgcaga	300
gccgtggcca gtacagctgc tctgggcagg tgatgtatat tccacagaca	350
ttcacacaaa cttcagagac tgccatgggt caagtccaag agctgtttcc	400
acctcctgtg ctgagtgcca tcccctctcc tgagccccga gagggtagcc	450
tggtgacct gagatgtcag acaaagctgc acccctgag gtcagccttg	500
aggtccttt tctccttoca caaggacggc cacacctgc aggacagggg	550
ccctcaccca gaactctgca tcccgggagc caaggagga gactctgggc	600
tttactggtg tgaggtggcc cctgagggtg gccaggcca gaagcagagc	650
ccccagctgg aggtcagagt gcaggtcct gtatcccgtc ctgtgtcac	700
tctgcaccac gggcctgctg accctgctgt gggggacatg gtgcagctcc	750
tctgtgaggc acagaggggc tcccctccga tctgtattc cttctacctt	800
gatgagaaga ttgtggggaa ccaactcagc cctgtgggtg gaaccacctc	850
cctcctcttc ccagtgaagt cagaacagga tgctgggaac tactcctgcg	900
aggctgagaa cagtgtctcc agagagagga gtgagcccaa gaagctgtct	950
ctgaaggggt ctcaagtctt gttcactccc gccagcaact ggctggttcc	1000
ttggcttcct gcgagcctgc ttggcctgat ggttattgct gctgcacttc	1050
tggtttatgt gagatcctgg agaaaagctg ggccccctcc atcccagata	1100
ccaccacag ctccaggtgg agagcagctc ccaactatag ccaacgtgca	1150
tcaccagaaa gggaaagatg aaggtgttgt ctactctgtg gtgcatagaa	1200
cctcaaagag gagtgaagga cagttctatc atctgtgctg aggtgagatg	1250
cctgcagccc agtgaggttt catccacgga ggtgaatatg agaagcagga	1300
ctctccaaga accccttagc gactgtgagg aggttctctg ctagtgatgg	1350
tgttctccta tcaacacacg cccaccccca gtctccagtg ctctcagga	1400
agacagtggt gtctcaact ctttctgtgg gtctctcagt tcccagccc	1450
agcatcacag agccccctga gcccttgctc tggtcaggag cacctgaacc	1500
ctgggttctt ttcttagcag aagaccaacc aatggaatgg gaagggagat	1550
gtccccacca acacacacac ttaggttcaa tcagtgcac tggacacata	1600
agccacagat gtcttcttcc catacaagca tgtagtctcg ccccaatata	1650
catatatata tgaatatgct atgtgccgca taacaacatt tcagtcatg	1700
atagactgca tacacaacag tggccccata agactgtaat ggagtttaaa	1750
aattcctact gcctagtgat atcatagttg ccttaacatc ataacacaac	1800
acatttctca cgcgtttgtg gtgatgctgg tacaacaag ctacagcgcc	1850

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 ctagtcata tacaatatata gcacatacaa ttatgtacag tacactatac 1900

ttgataatga taataaacaa ctatgttact ggt 1933

<210> SEQ ID NO 44

<211> LENGTH: 392

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 44

 Met Leu Pro Ser Leu Val Pro Cys Val Gly Lys Thr Val Trp Leu
 1 5 10 15

 Tyr Leu Gln Ala Trp Pro Asn Pro Val Phe Glu Gly Asp Ala Leu
 20 25 30

 Thr Leu Arg Cys Gln Gly Trp Lys Asn Thr Pro Leu Ser Gln Val
 35 40 45

 Lys Phe Tyr Arg Asp Gly Lys Phe Leu His Phe Ser Lys Glu Asn
 50 55 60

 Gln Thr Leu Ser Met Gly Ala Ala Thr Val Gln Ser Arg Gly Gln
 65 70 75

 Tyr Ser Cys Ser Gly Gln Val Met Tyr Ile Pro Gln Thr Phe Thr
 80 85 90

 Gln Thr Ser Glu Thr Ala Met Val Gln Val Gln Glu Leu Phe Pro
 95 100 105

 Pro Pro Val Leu Ser Ala Ile Pro Ser Pro Glu Pro Arg Glu Gly
 110 115 120

 Ser Leu Val Thr Leu Arg Cys Gln Thr Lys Leu His Pro Leu Arg
 125 130 135

 Ser Ala Leu Arg Leu Leu Phe Ser Phe His Lys Asp Gly His Thr
 140 145 150

 Leu Gln Asp Arg Gly Pro His Pro Glu Leu Cys Ile Pro Gly Ala
 155 160 165

 Lys Glu Gly Asp Ser Gly Leu Tyr Trp Cys Glu Val Ala Pro Glu
 170 175 180

 Gly Gly Gln Val Gln Lys Gln Ser Pro Gln Leu Glu Val Arg Val
 185 190 195

 Gln Ala Pro Val Ser Arg Pro Val Leu Thr Leu His His Gly Pro
 200 205 210

 Ala Asp Pro Ala Val Gly Asp Met Val Gln Leu Leu Cys Glu Ala
 215 220 225

 Gln Arg Gly Ser Pro Pro Ile Leu Tyr Ser Phe Tyr Leu Asp Glu
 230 235 240

 Lys Ile Val Gly Asn His Ser Ala Pro Cys Gly Gly Thr Thr Ser
 245 250 255

 Leu Leu Phe Pro Val Lys Ser Glu Gln Asp Ala Gly Asn Tyr Ser
 260 265 270

 Cys Glu Ala Glu Asn Ser Val Ser Arg Glu Arg Ser Glu Pro Lys
 275 280 285

 Lys Leu Ser Leu Lys Gly Ser Gln Val Leu Phe Thr Pro Ala Ser
 290 295 300

 Asn Trp Leu Val Pro Trp Leu Pro Ala Ser Leu Leu Gly Leu Met
 305 310 315

 Val Ile Ala Ala Ala Leu Leu Val Tyr Val Arg Ser Trp Arg Lys
 320 325 330

Ala Gly Pro Leu Pro Ser Gln Ile Pro Pro Thr Ala Pro Gly Gly

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	335		340		345									
Glu	Gln	Cys	Pro	Leu	Tyr	Ala	Asn	Val	His	His	Gln	Lys	Gly	Lys
				350					355					360
Asp	Glu	Gly	Val	Val	Tyr	Ser	Val	Val	His	Arg	Thr	Ser	Lys	Arg
				365					370					375
Ser	Glu	Gly	Gln	Phe	Tyr	His	Leu	Cys	Gly	Gly	Glu	Met	Pro	Ala
				380					385					390

Ala Gln

<210> SEQ ID NO 45
 <211> LENGTH: 900
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 45

```

ccattgttct caacattcta gctgctcttg ctgcatttgc tctggaattc          50
ttgtagagat attacttgtc cttccaggct gttctttctg tagctccctt          100
gttttctttt tgtgatcatg ttgcagatgg ctgggcagtg ctcccaaaat          150
gaatatattg acagtttggt gcatgcttgc ataccttgtc aacttcgatg          200
ttcttctaata actcctctctc taacatgtca gcggttattgt aatgcaagtg          250
tgaccaattc agtgaaagga acgaatgcga ttctctggac ctgtttggga          300
ctgagcttaa taatttcttt gccagtttct gtgctaattgt ttttgctaag          350
gaagataagc tctgaacat taaaggacga gtttaaaaac acaggatcag          400
gtctcctggg catggctaac attgacctgg aaaagagcag gactgggtgat          450
gaaattattc ttccgagagg cctcgagtac acggtggaag aatgcacctg          500
tgaagactgc atcaagagca aaccgaaggt cgactctgac cattgctttc          550
cactcccagc tatggaggaa ggcgcaacca ttcttgtcac cactgaaaacg          600
aatgactatt gcaagagcct gccagctgct ttgagtgcta cggagataga          650
gaaatcaatt tctgctaggt aattaacat ttcgactcga gcagtgccac          700
tttaaaaatc ttttgtcaga atagatgatg tgtcagatct ctttaggatg          750
actgtatttt tcagttgccg atacagcttt ttgtcctcta actgtggaaa          800
ctctttatgt tagatatatt tctctaggtt actgttggga gcttaatggt          850
agaaaacttc ttggtttcat gattaaagtc ttttttttct ctgaaaaaaa          900

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<210> SEQ ID NO 46
 <211> LENGTH: 184
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 46

Met	Leu	Gln	Met	Ala	Gly	Gln	Cys	Ser	Gln	Asn	Glu	Tyr	Phe	Asp
1			5						10					15
Ser	Leu	Leu	His	Ala	Cys	Ile	Pro	Cys	Gln	Leu	Arg	Cys	Ser	Ser
			20						25					30
Asn	Thr	Pro	Pro	Leu	Thr	Cys	Gln	Arg	Tyr	Cys	Asn	Ala	Ser	Val
				35					40					45
Thr	Asn	Ser	Val	Lys	Gly	Thr	Asn	Ala	Ile	Leu	Trp	Thr	Cys	Leu
				50					55					60
Gly	Leu	Ser	Leu	Ile	Ile	Ser	Leu	Ala	Val	Phe	Val	Leu	Met	Phe
				65					70					75

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Leu Leu Arg Lys Ile Ser Ser Glu Pro Leu Lys Asp Glu Phe Lys
 80 85 90
 Asn Thr Gly Ser Gly Leu Leu Gly Met Ala Asn Ile Asp Leu Glu
 95 100 105
 Lys Ser Arg Thr Gly Asp Glu Ile Ile Leu Pro Arg Gly Leu Glu
 110 115 120
 Tyr Thr Val Glu Glu Cys Thr Cys Glu Asp Cys Ile Lys Ser Lys
 125 130 135
 Pro Lys Val Asp Ser Asp His Cys Phe Pro Leu Pro Ala Met Glu
 140 145 150
 Glu Gly Ala Thr Ile Leu Val Thr Thr Lys Thr Asn Asp Tyr Cys
 155 160 165
 Lys Ser Leu Pro Ala Ala Leu Ser Ala Thr Glu Ile Glu Lys Ser
 170 175 180
 Ile Ser Ala Arg

<210> SEQ ID NO 47
 <211> LENGTH: 337
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: Unsure
 <222> LOCATION: 106, 108, 168, 298
 <223> OTHER INFORMATION: Unknown base

<400> SEQUENCE: 47

cttcccagcc ttcggaacta tggagcccgc actctccagt tcatcaccac 50
 cccagcatcc ctactcttgc atctaacagt ttccgctatt ttgcaccacc 100
 tgcttngnoc ttatgggcaa ctcaaggaag aaaggaaaga agagatagag 150
 gaaaaatgga ttcaacanat gaaagtgttc tttctgacta ctgctgtgtt 200
 tacaacatt ttaatcatca aaacatgctt tatttgatag aaagatcaaa 250
 tctgccttgg taaaacaaga gactatttta atcattaaga caacacanat 300
 gtttgatttg gaggcgtgtt ctcattcaaa accttgc 337

<210> SEQ ID NO 48
 <211> LENGTH: 1922
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 48

ggagagtctg accaccatgc cacctcctcg cctcctcttc ttctcctct 50
 tcctcaccoc catggaagtc aggcccagg aacctctagt ggtgaagggtg 100
 gaagagggtg ataacgctgt gctgcagtgc ctcaagggga cctcagatgg 150
 ccccactcag cagctgaact ggtctcggga gtccccgctt aaaccttct 200
 taaaactcag cctggggctg ccaggcctgg gaatccacat gaggeccctg 250
 gccatctggc ttttcatctt caacgtctct caacagatgg ggggcttcta 300
 cctgtgccag ccggggcccc cctctgagaa ggcctggcag cctggctgga 350
 cagtcaatgt ggagggcagc ggggagctgt tccggtggaa tgtttcggac 400
 ctagtggtcc tgggctgtgg cctgaagaac aggtcctcag agggccccag 450
 ctccccttcc gggaaactca tgagcccaaa gctgtatgtg tgggccaag 500
 accgccctga gatctgggag ggagagcctc cgtgtgtccc accgagggtc 550

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agcctgaacc agagcctcag ccaggacctc accatggccc ctggctccac      600
actctggctg tcctgtgggg taccacctga ctctgtgtcc aggggcccc      650
tctcctggac ccatgtgcac cccaaggggc ctaagtcatt gctgagccta      700
gagctgaagg acgatcgccc ggccagagat atgtgggtaa tggagacggg      750
tctgttgttg ccccgggcca cagctcaaga cgctggaaag tattattgtc      800
accgtggcaa cctgaccatg tcattccacc tggagatcac tgctcggcca      850
gtactatggc actggctgct gaggactggt ggctggaagg tctcagctgt      900
gactttggct tatctgatct tctgctgtg ttcccttggt ggcattcttc      950
atcttcaaag agccttggtc ctgaggagga aaagaaagcg aatgactgac     1000
cccaccagga gattcttcaa agtgacgctt ccccagga gcgggcccca     1050
gaaccagtac ggaacgtgc tgtctctccc cacaccacc tcaggcctcg     1100
gacgcgcccc gcgttgggcc gcaggcctgg ggggcactgc cccgtcttat     1150
ggaaacccca gcagcgacgt ccaggcggtt ggagccttgg ggtcccggag     1200
ccgccgggag tgggcccaga agaagaggaa ggggagggct atgaggaacc     1250
tgacagtgag gaggactccg agttctatga gaacgactcc aaccttgggc     1300
aggaccagct ctcccaggat ggcagcggtt acgagaacct tgaggatgag     1350
cccctgggtc ctgaggatga agactccttc tccaacgctg agtcttatga     1400
gaacgaggat gaagagctga cccagccggt cgccaggaca atggacttcc     1450
tgagccctca tgggtcagcc tgggacccca gccgggaagc aacctccctg     1500
gggtcccagt cctatgagga tatgagagga atcctgtatg cagcccccca     1550
gctccgctcc attcggggcc agcctggacc caatcatgag gaagatgcag     1600
actcttatga gaacatggat aatcccgatg ggcagacccc agcctgggga     1650
ggagggggcc gcatgggcac ctggagcacc aggtgatcct caggtggcca     1700
gcctggatct cctcaagtcc ccaagattca cacctgactc tgaaatctga     1750
agacctcgag cagatgatgc caacctctgg agcaatgttg cttaggatgt     1800
gtgcatgtgt gtaagtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtat     1850
acatgccagt gacacttcca gtcccccttg tattccttaa ataaactcaa     1900
tgagctcttc caaaaaaaaa aa                                  1922

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<210> SEQ ID NO 49

<211> LENGTH: 467

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 49

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Met Pro Pro Pro Arg Leu Leu Phe Phe Leu Leu Phe Leu Thr Pro
 1           5           10          15
Met Glu Val Arg Pro Glu Glu Pro Leu Val Val Lys Val Glu Glu
          20           25           30
Gly Asp Asn Ala Val Leu Gln Cys Leu Lys Gly Thr Ser Asp Gly
          35           40           45
Pro Thr Gln Gln Leu Thr Trp Ser Arg Glu Ser Pro Leu Lys Pro
          50           55           60
Phe Leu Lys Leu Ser Leu Gly Leu Pro Gly Leu Gly Ile His Met
          65           70           75

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Arg	Pro	Leu	Ala	Ile	Trp	Leu	Phe	Ile	Phe	Asn	Val	Ser	Gln	Gln	80	85	90
Met	Gly	Gly	Phe	Tyr	Leu	Cys	Gln	Pro	Gly	Pro	Pro	Ser	Glu	Lys	95	100	105
Ala	Trp	Gln	Pro	Gly	Trp	Thr	Val	Asn	Val	Glu	Gly	Ser	Gly	Glu	110	115	120
Leu	Phe	Arg	Trp	Asn	Val	Ser	Asp	Leu	Gly	Gly	Leu	Gly	Cys	Gly	125	130	135
Leu	Lys	Asn	Arg	Ser	Ser	Glu	Gly	Pro	Ser	Ser	Pro	Ser	Gly	Lys	140	145	150
Leu	Met	Ser	Pro	Lys	Leu	Tyr	Val	Trp	Ala	Lys	Asp	Arg	Pro	Glu	155	160	165
Ile	Trp	Glu	Gly	Glu	Pro	Pro	Cys	Val	Pro	Pro	Arg	Asp	Ser	Leu	170	175	180
Asn	Gln	Ser	Leu	Ser	Gln	Asp	Leu	Thr	Met	Ala	Pro	Gly	Ser	Thr	185	190	195
Leu	Trp	Leu	Ser	Cys	Gly	Val	Pro	Pro	Asp	Ser	Val	Ser	Arg	Gly	200	205	210
Pro	Leu	Ser	Trp	Thr	His	Val	His	Pro	Lys	Gly	Pro	Lys	Ser	Leu	215	220	225
Leu	Ser	Leu	Glu	Leu	Lys	Asp	Asp	Arg	Pro	Ala	Arg	Asp	Met	Trp	230	235	240
Val	Met	Glu	Thr	Gly	Leu	Leu	Leu	Pro	Arg	Ala	Thr	Ala	Gln	Asp	245	250	255
Ala	Gly	Lys	Tyr	Tyr	Cys	His	Arg	Gly	Asn	Leu	Thr	Met	Ser	Phe	260	265	270
His	Leu	Glu	Ile	Thr	Ala	Arg	Pro	Val	Leu	Trp	His	Trp	Leu	Leu	275	280	285
Arg	Thr	Gly	Gly	Trp	Lys	Val	Ser	Ala	Val	Thr	Leu	Ala	Tyr	Leu	290	295	300
Ile	Phe	Cys	Leu	Cys	Ser	Leu	Val	Gly	Ile	Leu	His	Leu	Gln	Arg	305	310	315
Ala	Leu	Val	Leu	Arg	Arg	Lys	Arg	Lys	Arg	Met	Thr	Asp	Pro	Thr	320	325	330
Arg	Arg	Phe	Phe	Lys	Val	Thr	Pro	Pro	Pro	Gly	Ser	Gly	Pro	Gln	335	340	345
Asn	Gln	Tyr	Gly	Asn	Val	Leu	Ser	Leu	Pro	Thr	Pro	Thr	Ser	Gly	350	355	360
Leu	Gly	Arg	Ala	Gln	Arg	Trp	Ala	Ala	Gly	Leu	Gly	Gly	Thr	Ala	365	370	375
Pro	Ser	Tyr	Gly	Asn	Pro	Ser	Ser	Asp	Val	Gln	Ala	Asp	Gly	Ala	380	385	390
Leu	Gly	Ser	Arg	Ser	Arg	Arg	Glu	Trp	Ala	Gln	Lys	Lys	Arg	Lys	395	400	405
Gly	Arg	Ala	Met	Arg	Asn	Leu	Thr	Val	Arg	Arg	Thr	Pro	Ser	Ser	410	415	420
Met	Arg	Thr	Thr	Pro	Thr	Leu	Gly	Arg	Thr	Ser	Ser	Pro	Arg	Met	425	430	435
Ala	Ala	Ala	Thr	Arg	Thr	Leu	Arg	Met	Ser	Pro	Trp	Val	Leu	Arg	440	445	450
Met	Lys	Thr	Pro	Ser	Pro	Thr	Leu	Ser	Leu	Met	Arg	Thr	Arg	Met	455	460	465

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Lys Ser

<210> SEQ ID NO 50

<211> LENGTH: 3260

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 50

ccatcccata	gtgaggggaag	acacgcggaa	acaggcttgc	acccagacac	50
gacaccatgc	atctcctcgg	cccctggctc	ctgctcctgg	ttctagaata	100
cttggtcttc	tctgactcaa	gtaaattgggt	ttttgagcac	cctgaaaccc	150
tctacgcctg	ggagggggcc	tgcgtctgga	tcccctgcac	ctacagagcc	200
ctagatggtg	acctggaaag	cttcatcctg	ttccacaatc	ctgagtataa	250
caagaacacc	tcgaagtttg	atgggacaag	actctatgaa	agcaciaaag	300
atgggaaggt	tccttctgag	cagaaaaggg	tgcaattcct	gggagacaag	350
aataagaact	gcacactgag	tatccacccg	gtgcaacctc	atgacagtgg	400
tcagctgggg	ctgaggatgg	agtccaagac	tgagaaatgg	atggaacgaa	450
tacacctcaa	tgtctctgaa	aggccttttc	cacctcatat	ccagctccct	500
ccagaaattc	aagagtccca	ggaagtcact	ctgacctgct	tgctgaattt	550
ctcctgctat	gggtatecga	tccaattgca	gtggctccta	gagggggttc	600
caatgaggca	ggctgctgtc	acctcgacct	ccttgacct	caagtctgtc	650
ttcaccggga	gcgagctcaa	gttctcccca	cagtgagctc	accatgggaa	700
gattgtgacc	tgccagcttc	aggatgcaga	tgggaagttc	ctctccaatg	750
acacggtgca	gctgaacgtg	aagcacaccc	cgaagtggga	gatcaaggtc	800
actcccagtg	atgccatagt	gagggagggg	gactctgtga	ccatgacctg	850
cgaggtcagc	agcagcaacc	cggagtacac	gacggtatcc	tggtcaagg	900
atgggacctc	gctgaagaag	cagaatacat	tcacgctaaa	cctgcccgaa	950
gtgaccaagg	accagagtgg	gaagtactgc	tgtcaggtct	ccaatgacgt	1000
gggcccggga	aggtcggaag	aagtgttctc	gcaagtgcag	tatgccccgg	1050
aaccttccac	ggttcagatc	ctccactcac	cggctgtgga	gggaagtcaa	1100
gtcaggtttc	tttgcattgc	actggccaat	cctcttccaa	caaattacac	1150
gtggtaccac	aatgggaaag	aatgcaggg	aaggacagag	gagaaagtcc	1200
acatcccaaa	gatcctcccc	tggcacgctg	ggacttattc	ctgtgtggca	1250
gaaaacattc	ttggtactgg	acagaggggc	ccgggagctg	agctggatgt	1300
ccagtatcct	cccagaagag	tgaccacagt	gattcaaac	cccagccga	1350
ttcgagaagg	agacacagtg	accctttcct	gtaactacaa	ttccagtaac	1400
cccagtgta	cccggatga	atgaaaacc	catggcgctc	gggaggagcc	1450
atcgcttggg	gtgctgaaga	tccaaaacgt	tggctgggac	aacacaacca	1500
tcgcctgcgc	acgttgtaat	agttggtgct	cgtgggcctc	ccctgtcgcc	1550
ctgaatgtcc	agtatgcccc	ccgagacgtg	agggtccgga	aaatcaagcc	1600
cctttccgag	atcactctg	gaaactcgg	cagctcccaa	tgtgacttct	1650
caagcagcca	ccccaaagaa	gtccagttct	tctgggagaa	aaatggcagg	1700
cttctgggga	aagaaagcca	gctgaatttt	gactccatct	cccagaaga	1750

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tgctgggagt tacagctgct gggtgaacaa ctccatagga cagacagcgt      1800
ccaaggcctg gacacttgaa gtgctgtatg caccaggag gctgcgtgtg      1850
tccatgagcc cgggggacca agtgatggag ggaagagtg caaccctgac      1900
ctgtgagagt gacgccaacc ctcccgcttc ccactacacc tggtttgact      1950
ggaataacca aagcctcccc caccacagcc agaagctgag attggagccg      2000
gtgaaggtcc agcactcggg tgccactcgg tgccagggga ccaacagtgt      2050
gggcaagggc cgttcgcctc tcagcaccct tactgtctac tatagccggg      2100
agaccatcgg caggcgagtg gctgtgggac tcgggtcctg cctcgccatc      2150
ctcatcctgg caatctgtgg gctcaagctc cagcgacgtt ggaagaggac      2200
acagagccag caggggcttc aggagaattc cagcggccag agcttctttg      2250
tgaggaataa aaaggttaga agggcccccc tctctgaagg cccccactcc      2300
ctgggatgct acaatccaat gatggaagat ggcattagct acaccacctt      2350
gcgctttccc gagatgaaca taccacgaac tggagatgca gagtccctcag      2400
agatgcagag acctccccgg acctgcgatg acacggtcac ttattcagca      2450
ttgcacaagc gccaaagtgg cgactatgag aacgtcattc cagattttcc      2500
agaagatgag gggattcatt actcagagct gatccagttt ggggtcgggg      2550
agcggcctca ggcacaagaa aatgtggact atgtgatcct caaacattga      2600
cactggatgg gctgcagcag aggcactggg ggcagcgggg gccaggggaag      2650
tccccgagtt tccccagaca ccgccacatg gcttctcctt gcgtgcatgt      2700
gcgcacacac acacacacac gcacacacac acacacacac tcactgcgga      2750
gaaacctgtg cctggctcag agccagtctt ttggtgagg gtaaccccaa      2800
acctccaaaa ctctgcccc tgtctctctc cactctcctt gctaccaga      2850
aatcatctaa atacctgccc tgacatgac acctcccctg ccccaccagc      2900
ccactggcca tctccaccg gagctgctgt gtcctctgga tctgctcgtc      2950
atcttctctc ccttctccat ctctctggcc ctctaccctt gatctgacat      3000
ccccactcac gaatattatg ccagtttct gcctctgagg gaaagcccag      3050
aaaaggacag aaacgaagta gaaaggggcc cagtcctggc ctggcttctc      3100
ctttggaagt gaggcattgc acggggagac gtacgtatca ggggccctt      3150
gactctgggg actccgggtt tgagatggac aactgggtgt ggattaacct      3200
gccagggaga cagagctcac aataaaaatg gctcagatgc cacttcaaag      3250
aaaaaaaaaa                                     3260

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<210> SEQ ID NO 51

<211> LENGTH: 847

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 51

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Met His Leu Leu Gly Pro Trp Leu Leu Leu Leu Val Leu Glu Tyr
  1             5             10             15
Leu Ala Phe Ser Asp Ser Ser Lys Trp Val Phe Glu His Pro Glu
             20             25             30
Thr Leu Tyr Ala Trp Glu Gly Ala Cys Val Trp Ile Pro Cys Thr
             35             40             45

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Tyr	Arg	Ala	Leu	Asp	Gly	Asp	Leu	Glu	Ser	Phe	Ile	Leu	Phe	His
				50					55					60
Asn	Pro	Glu	Tyr	Asn	Lys	Asn	Thr	Ser	Lys	Phe	Asp	Gly	Thr	Arg
				65					70					75
Leu	Tyr	Glu	Ser	Thr	Lys	Asp	Gly	Lys	Val	Pro	Ser	Glu	Gln	Lys
				80					85					90
Arg	Val	Gln	Phe	Leu	Gly	Asp	Lys	Asn	Lys	Asn	Cys	Thr	Leu	Ser
				95					100					105
Ile	His	Pro	Val	His	Leu	Asn	Asp	Ser	Gly	Gln	Leu	Gly	Leu	Arg
				110					115					120
Met	Glu	Ser	Lys	Thr	Glu	Lys	Trp	Met	Glu	Arg	Ile	His	Leu	Asn
				125					130					135
Val	Ser	Glu	Arg	Pro	Phe	Pro	Pro	His	Ile	Gln	Leu	Pro	Pro	Glu
				140					145					150
Ile	Gln	Glu	Ser	Gln	Glu	Val	Thr	Leu	Thr	Cys	Leu	Leu	Asn	Phe
				155					160					165
Ser	Cys	Tyr	Gly	Tyr	Pro	Ile	Gln	Leu	Gln	Trp	Leu	Leu	Glu	Gly
				170					175					180
Val	Pro	Met	Arg	Gln	Ala	Ala	Val	Thr	Ser	Thr	Ser	Leu	Thr	Ile
				185					190					195
Lys	Ser	Val	Phe	Thr	Arg	Ser	Glu	Leu	Lys	Phe	Ser	Pro	Gln	Trp
				200					205					210
Ser	His	His	Gly	Lys	Ile	Val	Thr	Cys	Gln	Leu	Gln	Asp	Ala	Asp
				215					220					225
Gly	Lys	Phe	Leu	Ser	Asn	Asp	Thr	Val	Gln	Leu	Asn	Val	Lys	His
				230					235					240
Thr	Pro	Lys	Leu	Glu	Ile	Lys	Val	Thr	Pro	Ser	Asp	Ala	Ile	Val
				245					250					255
Arg	Glu	Gly	Asp	Ser	Val	Thr	Met	Thr	Cys	Glu	Val	Ser	Ser	Ser
				260					265					270
Asn	Pro	Glu	Tyr	Thr	Thr	Val	Ser	Trp	Leu	Lys	Asp	Gly	Thr	Ser
				275					280					285
Leu	Lys	Lys	Gln	Asn	Thr	Phe	Thr	Leu	Asn	Leu	Arg	Glu	Val	Thr
				290					295					300
Lys	Asp	Gln	Ser	Gly	Lys	Tyr	Cys	Cys	Gln	Val	Ser	Asn	Asp	Val
				305					310					315
Gly	Pro	Gly	Arg	Ser	Glu	Glu	Val	Phe	Leu	Gln	Val	Gln	Tyr	Ala
				320					325					330
Pro	Glu	Pro	Ser	Thr	Val	Gln	Ile	Leu	His	Ser	Pro	Ala	Val	Glu
				335					340					345
Gly	Ser	Gln	Val	Glu	Phe	Leu	Cys	Met	Ser	Leu	Ala	Asn	Pro	Leu
				350					355					360
Pro	Thr	Asn	Tyr	Thr	Trp	Tyr	His	Asn	Gly	Lys	Glu	Met	Gln	Gly
				365					370					375
Arg	Thr	Glu	Glu	Lys	Val	His	Ile	Pro	Lys	Ile	Leu	Pro	Trp	His
				380					385					390
Ala	Gly	Thr	Tyr	Ser	Cys	Val	Ala	Glu	Asn	Ile	Leu	Gly	Thr	Gly
				395					400					405
Gln	Arg	Gly	Pro	Gly	Ala	Glu	Leu	Asp	Val	Gln	Tyr	Pro	Pro	Lys
				410					415					420
Lys	Val	Thr	Thr	Val	Ile	Gln	Asn	Pro	Met	Pro	Ile	Arg	Glu	Gly
				425					430					435

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Asp	Thr	Val	Thr	Leu	Ser	Cys	Asn	Tyr	Asn	Ser	Ser	Asn	Pro	Ser	
				440					445					450	
Val	Thr	Arg	Tyr	Glu	Trp	Lys	Pro	His	Gly	Ala	Trp	Glu	Glu	Pro	
				455					460					465	
Ser	Leu	Gly	Val	Leu	Lys	Ile	Gln	Asn	Val	Gly	Trp	Asp	Asn	Thr	
				470					475					480	
Thr	Ile	Ala	Cys	Ala	Arg	Cys	Asn	Ser	Trp	Cys	Ser	Trp	Ala	Ser	
				485					490					495	
Pro	Val	Ala	Leu	Asn	Val	Gln	Tyr	Ala	Pro	Arg	Asp	Val	Arg	Val	
				500					505					510	
Arg	Lys	Ile	Lys	Pro	Leu	Ser	Glu	Ile	His	Ser	Gly	Asn	Ser	Val	
				515					520					525	
Ser	Leu	Gln	Cys	Asp	Phe	Ser	Ser	Ser	His	Pro	Lys	Glu	Val	Gln	
				530					535					540	
Phe	Phe	Trp	Glu	Lys	Asn	Gly	Arg	Leu	Leu	Gly	Lys	Glu	Ser	Gln	
				545					550					555	
Leu	Asn	Phe	Asp	Ser	Ile	Ser	Pro	Glu	Asp	Ala	Gly	Ser	Tyr	Ser	
				560					565					570	
Cys	Trp	Val	Asn	Asn	Ser	Ile	Gly	Gln	Thr	Ala	Ser	Lys	Ala	Trp	
				575					580					585	
Thr	Leu	Glu	Val	Leu	Tyr	Ala	Pro	Arg	Arg	Leu	Arg	Val	Ser	Met	
				590					595					600	
Ser	Pro	Gly	Asp	Gln	Val	Met	Glu	Gly	Lys	Ser	Ala	Thr	Leu	Thr	
				605					610					615	
Cys	Glu	Ser	Asp	Ala	Asn	Pro	Pro	Val	Ser	His	Tyr	Thr	Trp	Phe	
				620					625					630	
Asp	Trp	Asn	Asn	Gln	Ser	Leu	Pro	His	His	Ser	Gln	Lys	Leu	Arg	
				635					640					645	
Leu	Glu	Pro	Val	Lys	Val	Gln	His	Ser	Gly	Ala	Tyr	Trp	Cys	Gln	
				650					655					660	
Gly	Thr	Asn	Ser	Val	Gly	Lys	Gly	Arg	Ser	Pro	Leu	Ser	Thr	Leu	
				665					670					675	
Thr	Val	Tyr	Tyr	Ser	Pro	Glu	Thr	Ile	Gly	Arg	Arg	Val	Ala	Val	
				680					685					690	
Gly	Leu	Gly	Ser	Cys	Leu	Ala	Ile	Leu	Ile	Leu	Ala	Ile	Cys	Gly	
				695					700					705	
Leu	Lys	Leu	Gln	Arg	Arg	Trp	Lys	Arg	Thr	Gln	Ser	Gln	Gln	Gly	
				710					715					720	
Leu	Gln	Glu	Asn	Ser	Ser	Gly	Gln	Ser	Phe	Phe	Val	Arg	Asn	Lys	
				725					730					735	
Lys	Val	Arg	Arg	Ala	Pro	Leu	Ser	Glu	Gly	Pro	His	Ser	Leu	Gly	
				740					745					750	
Cys	Tyr	Asn	Pro	Met	Met	Glu	Asp	Gly	Ile	Ser	Tyr	Thr	Thr	Leu	
				755					760					765	
Arg	Phe	Pro	Glu	Met	Asn	Ile	Pro	Arg	Thr	Gly	Asp	Ala	Glu	Ser	
				770					775					780	
Ser	Glu	Met	Gln	Arg	Pro	Pro	Arg	Thr	Cys	Asp	Asp	Thr	Val	Thr	
				785					790					795	
Tyr	Ser	Ala	Leu	His	Lys	Arg	Gln	Val	Gly	Asp	Tyr	Glu	Asn	Val	
				800					805					810	
Ile	Pro	Asp	Phe	Pro	Glu	Asp	Glu	Gly	Ile	His	Tyr	Ser	Glu	Leu	
				815					820					825	
Ile	Gln	Phe	Gly	Val	Gly	Glu	Arg	Pro	Gln	Ala	Gln	Glu	Asn	Val	

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	830	835	840	
Asp Tyr Val Ile Leu Lys His				
	845			
<210> SEQ ID NO 52				
<211> LENGTH: 1670				
<212> TYPE: DNA				
<213> ORGANISM: Homo sapiens				
<400> SEQUENCE: 52				
ccaaccacaa gcaccaaagc agaggggcag gcagcacacc acccagcagc				50
cagagcacca gccagccat ggtccttgag gtgagtgacc accaagtgct				100
aatgacgcc gaggttgccg ccctcctgga gaacttcagc tcttctatg				150
actatggaga aaacgagagt gactcgtgct gtacctcccc gccctgcccc				200
caggacttca gcctgaactt cgaccgggcc ttcctgccag ccctctacag				250
cctcctcttt ctgctggggc tgctgggcaa cggcgcggtg gcagccgtgc				300
tgctgagccg gcggacagcc ctgagcagca ccgacacctt cctgctccac				350
ctagctgtag cagacacgct gctggtgctg acaactgccg tctgggcagt				400
ggacgctgcc gtccagtggg tctttggctc tggcctctgc aaagtggcag				450
gtgccctctt caacatcaac ttctacgcag gagecctcct gctggcctgc				500
atcagctttg accgctacct gaacatagtt catgccacct agctctaccg				550
ccgggggccc ccggcccgcg tgacctcac ctgcctggct gtctgggggc				600
tctgcctgct tttcgccctc ccagacttca tcttctctgc ggcccaccac				650
gacgagcgc tcaacgccac ccactgccaa tacaacttcc cacaggtggg				700
ccgcacggct ctgcgggtgc tgcagctggt ggctggcttt ctgctgcccc				750
tgctggctcat ggctactgc tatgccacaca tccctggcct gctgctggtt				800
tccaggggcc agcggcgccct gcgggcoatg cggctggtgg tgggtggtcgt				850
ggtggccttt gccctctgct ggacccccta tcacctggtg gtgctggtgg				900
acatcctcat ggacctgggc gctttggccc gcaactgtgg ccgagaaagc				950
agggtagacg tggccaagtc ggtcacctca gccctgggct acatgcactg				1000
ctgcctcaac ccgctgctct atgcctttgt aggggtcaag ttccgggagc				1050
ggatgtggat gctgctcttg cgctgggct gccccaacca gagagggctc				1100
cagaggcagc catcgtcttc ccgccgggat tcacctcggg ctgagacctc				1150
agaggcctcc tactcgggct tgtgaggccg gaatecgggc tccccttctg				1200
cccacagtct gaattccccg cattccaggc tectcctccc ctctgccggc				1250
tctggctctc cccaatatcc tcgctcccgg gactcactgg cagccccagc				1300
accaccaggt ctcccgggaa gccacctcc cagctctgag gactgcacca				1350
ttgctgctcc ttagctgcca agccccatcc tgccgcccga ggtggctgcc				1400
tggagcccca ctgcccttct catttggaat ctaaaacttc atcttcccca				1450
agtgcgggga gtacaaggca tggcgtagag ggtgctgccc catgaagcca				1500
cagcccaggc ctccagctca gcagtgactg tggccatggt cccaagacc				1550
tctatatttg ctcttttatt tttatgtcta aaatcctgct taaaactttt				1600
caataaacaa gatcgtcagg accaaaaaaaa aaaaaaaaaa aaaaaaaaaa				1650

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aaaaaaaaa aaaaaaaaaa

1670

<210> SEQ ID NO 53

<211> LENGTH: 368

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 53

```

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu
 1          5          10          15
Val Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly
          20          25          30
Glu Asn Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln
          35          40          45
Asp Phe Ser Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr
          50          55          60
Ser Leu Leu Phe Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala
          65          70          75
Ala Val Leu Leu Ser Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr
          80          85          90
Phe Leu Leu His Leu Ala Val Ala Asp Thr Leu Leu Val Leu Thr
          95          100          105
Leu Pro Leu Trp Ala Val Asp Ala Ala Val Gln Trp Val Phe Gly
          110          115          120
Ser Gly Leu Cys Lys Val Ala Gly Ala Leu Phe Asn Ile Asn Phe
          125          130          135
Tyr Ala Gly Ala Leu Leu Leu Ala Cys Ile Ser Phe Asp Arg Tyr
          140          145          150
Leu Asn Ile Val His Ala Thr Gln Leu Tyr Arg Arg Gly Pro Pro
          155          160          165
Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp Gly Leu Cys Leu
          170          175          180
Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala His His Asp
          185          190          195
Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro Gln Val
          200          205          210
Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe Leu
          215          220          225
Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
          230          235          240
Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg
          245          250          255
Leu Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro
          260          265          270
Tyr His Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala
          275          280          285
Leu Ala Arg Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys
          290          295          300
Ser Val Thr Ser Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro
          305          310          315
Leu Leu Tyr Ala Phe Val Gly Val Lys Phe Arg Glu Arg Met Trp
          320          325          330
Met Leu Leu Leu Arg Leu Gly Cys Pro Asn Gln Arg Gly Leu Gln
          335          340          345

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Arg Gln Pro Ser Ser Ser Arg Arg Asp Ser Ser Trp Ser Glu Thr
 350 355 360

Ser Glu Ala Ser Tyr Ser Gly Leu
 365

<210> SEQ ID NO 54

<211> LENGTH: 2109

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 54

gaggaagaa cacaatggat ctggtgctaa aaagatgcct tcttcatttg	50
gctgtgatag gtgctttgct ggctgtgggg gctacaaaag taccagaaa	100
ccaggactgg cttggtgtct caaggcaact cagaaccaa gcctggaaca	150
ggcagctgta tccagagtgg acagaagccc agagacttga ctgctggaga	200
ggtggtcaag tgtccctcaa ggtcagtaat gatgggccta cactgattgg	250
tgcaaatgcc tccttctcta ttgcttgaa ctccctgga agccaaaagg	300
tattgccaga tgggcagggt atctgggtca acaatccat catcaatggg	350
agccagggtg ggggaggaca gccagtgtat ccccaggaaa ctgacgatgc	400
ctgcatcttc cctgatggtg gacctgccc atctggtctc tggctcaga	450
agagaagctt tgtttatgtc tggaagacct ggggccaata ctggcaagtt	500
ctagggggcc cagtgtctgg gctgagcatt gggacaggca gggcaatgct	550
gggcacacac accatggaag tgactgteta ccatcgccgg ggatcccga	600
gctatgtgcc tcttgctcat tccagctcag ccttccat tactgaccag	650
gtgcctttct cegtgagcgt gtcccagttg cgggccttgg atggaggaa	700
caagcacttc ctgagaaatc agcctctgac ctttgccctc cagctccatg	750
acccagtggt ctatctggct gaagctgacc tctcctacac ctgggaactt	800
ggagacagta gtggaacct gatctctcgg gcaactgttg tcaactatac	850
ttacctggag cctggcccag tcaactgcca ggtggtcctg caggctgcca	900
ttcctctcac ctctgtggc tcctccccag ttccaggcac cacagatggg	950
cacaggccaa ctgcagaggc cctaacacc acagctggcc aagtgcctac	1000
tacagaagtt gtgggtaact cacctgggtca ggcgccaact gcagagccct	1050
ctggaaccac atctgtgcag gtgccaacca ctgaagtcac aagcactgca	1100
cctgtgcaga tgccaactgc agagagcaca ggtatgacac ctgagaaggt	1150
gccagtttca gaggtcatgg gtaccacact ggcagagatg tcaactccag	1200
aggctacagg tatgacacct gcagaggat caattgtggt gctttctgga	1250
accacagctg cacaggtaac aactacagag tgggtggaga ccacagctag	1300
agagctacct atccctgagc ctgaaggtcc agatgccagc tcaatcatgt	1350
ctacggaaag tattacaggt tcctggggcc ccctgctgga tggtagagcc	1400
accttaaggc tgggtaagag acaagtcccc ctggattgtg ttctgtatcg	1450
atatggttcc ttttccgtca cctggacat tgtccagggt attgaaagtg	1500
ccgagatcct gcaggctgtg ccgtccgggt agggggatgc atttgagctg	1550
actgtgtcct gccaaaggcg gctgcccagg gaagcctgca tggagatctc	1600
atcgccaggg tgccagcccc ctgcccagcg gctgtgccag cctgtgctac	1650

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ccagcccagc ctgccagctg gttctgcacc agatactgaa gggtaggctcg      1700
gggacatact gcctcaatgt gtctctggct gataccaaca gcctggcagt      1750
ggtcagcacc cagcttatca tgccctgtca agaagcaggc cttgggcagg      1800
ttccgctgat cgtgggcate ttgctgggtg tgatggctgt ggtecttgca      1850
tctctgatat ataggcgcag acttatgaag caagacttct ccgtacccca      1900
gttgccacat agcagcagtc actggctgcg tctaccccgc atcttctgct      1950
cttgtcccat tggtgagaac agccccctcc tcagtgggca gcaggtctga      2000
gtactctcat atgatgctgt gattttctct gagttgacag aaacacctat      2050
atttcccca gtcttccctg ggagactact attaactgaa ataaatactc      2100
agagcctga      2109

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<210> SEQ ID NO 55

<211> LENGTH: 661

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 55

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Met Asp Leu Val Leu Lys Arg Cys Leu Leu His Leu Ala Val Ile
  1           5           10           15
Gly Ala Leu Leu Ala Val Gly Ala Thr Lys Val Pro Arg Asn Gln
          20           25           30
Asp Trp Leu Gly Val Ser Arg Gln Leu Arg Thr Lys Ala Trp Asn
          35           40           45
Arg Gln Leu Tyr Pro Glu Trp Thr Glu Ala Gln Arg Leu Asp Cys
          50           55           60
Trp Arg Gly Gly Gln Val Ser Leu Lys Val Ser Asn Asp Gly Pro
          65           70           75
Thr Leu Ile Gly Ala Asn Ala Ser Phe Ser Ile Ala Leu Asn Phe
          80           85           90
Pro Gly Ser Gln Lys Val Leu Pro Asp Gly Gln Val Ile Trp Val
          95          100          105
Asn Asn Thr Ile Ile Asn Gly Ser Gln Val Trp Gly Gly Gln Pro
          110          115          120
Val Tyr Pro Gln Glu Thr Asp Asp Ala Cys Ile Phe Pro Asp Gly
          125          130          135
Gly Pro Cys Pro Ser Gly Ser Trp Ser Gln Lys Arg Ser Phe Val
          140          145          150
Tyr Val Trp Lys Thr Trp Gly Gln Tyr Trp Gln Val Leu Gly Gly
          155          160          165
Pro Val Ser Gly Leu Ser Ile Gly Thr Gly Arg Ala Met Leu Gly
          170          175          180
Thr His Thr Met Glu Val Thr Val Tyr His Arg Arg Gly Ser Arg
          185          190          195
Ser Tyr Val Pro Leu Ala His Ser Ser Ser Ala Phe Thr Ile Thr
          200          205          210
Asp Gln Val Pro Phe Ser Val Ser Val Ser Gln Leu Arg Ala Leu
          215          220          225
Asp Gly Gly Asn Lys His Phe Leu Arg Asn Gln Pro Leu Thr Phe
          230          235          240
Ala Leu Gln Leu His Asp Pro Ser Gly Tyr Leu Ala Glu Ala Asp
          245          250          255

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Leu Ser Tyr Thr Trp Asp Phe Gly Asp Ser Ser Gly Thr Leu Ile
 260 265 270
 Ser Arg Ala Leu Val Val Thr His Thr Tyr Leu Glu Pro Gly Pro
 275 280 285
 Val Thr Ala Gln Val Val Leu Gln Ala Ala Ile Pro Leu Thr Ser
 290 295 300
 Cys Gly Ser Ser Pro Val Pro Gly Thr Thr Asp Gly His Arg Pro
 305 310 315
 Thr Ala Glu Ala Pro Asn Thr Thr Ala Gly Gln Val Pro Thr Thr
 320 325 330
 Glu Val Val Gly Thr Thr Pro Gly Gln Ala Pro Thr Ala Glu Pro
 335 340 345
 Ser Gly Thr Thr Ser Val Gln Val Pro Thr Thr Glu Val Ile Ser
 350 355 360
 Thr Ala Pro Val Gln Met Pro Thr Ala Glu Ser Thr Gly Met Thr
 365 370 375
 Pro Glu Lys Val Pro Val Ser Glu Val Met Gly Thr Thr Leu Ala
 380 385 390
 Glu Met Ser Thr Pro Glu Ala Thr Gly Met Thr Pro Ala Glu Val
 395 400 405
 Ser Ile Val Val Leu Ser Gly Thr Thr Ala Ala Gln Val Thr Thr
 410 415 420
 Thr Glu Trp Val Glu Thr Thr Ala Arg Glu Leu Pro Ile Pro Glu
 425 430 435
 Pro Glu Gly Pro Asp Ala Ser Ser Ile Met Ser Thr Glu Ser Ile
 440 445 450
 Thr Gly Ser Leu Gly Pro Leu Leu Asp Gly Thr Ala Thr Leu Arg
 455 460 465
 Leu Val Lys Arg Gln Val Pro Leu Asp Cys Val Leu Tyr Arg Tyr
 470 475 480
 Gly Ser Phe Ser Val Thr Leu Asp Ile Val Gln Gly Ile Glu Ser
 485 490 495
 Ala Glu Ile Leu Gln Ala Val Pro Ser Gly Glu Gly Asp Ala Phe
 500 505 510
 Glu Leu Thr Val Ser Cys Gln Gly Gly Leu Pro Lys Glu Ala Cys
 515 520 525
 Met Glu Ile Ser Ser Pro Gly Cys Gln Pro Pro Ala Gln Arg Leu
 530 535 540
 Cys Gln Pro Val Leu Pro Ser Pro Ala Cys Gln Leu Val Leu His
 545 550 555
 Gln Ile Leu Lys Gly Gly Ser Gly Thr Tyr Cys Leu Asn Val Ser
 560 565 570
 Leu Ala Asp Thr Asn Ser Leu Ala Val Val Ser Thr Gln Leu Ile
 575 580 585
 Met Pro Gly Gln Glu Ala Gly Leu Gly Gln Val Pro Leu Ile Val
 590 595 600
 Gly Ile Leu Leu Val Leu Met Ala Val Val Leu Ala Ser Leu Ile
 605 610 615
 Tyr Arg Arg Arg Leu Met Lys Gln Asp Phe Ser Val Pro Gln Leu
 620 625 630
 Pro His Ser Ser Ser His Trp Leu Arg Leu Pro Arg Ile Phe Cys
 635 640 645

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ttctctgggc caccgtgggg gcacctctgg cctcccgtga cccccaggcc 1700
gaggggtcccc gggcaccag gtcggtaaac tctcgccct ctcaggcccc 1750
cgtctctgcc tggaggagac tgtgtagggt ccggcgtggg gatcagccgg 1800
gatgggctgc gcgtctccag cctctgcaca cacattggcg ggtgggggtgc 1850
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gccaaggctc ggacgaggag agcgtgcata gcgacactcg ggacctgtgg 2100
accacgacca cgctgtccca ggcacagctg aacatgccgc tgtccgaggt 2150
ctgagggggc ttcgacgagg agggccgcaa cattagcaag acccgcggt 2200
ggcacagccc ggggcggggc tcgttgagc aggggtacaa ggccagccac 2250
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tcgagggcca aaagtcttc tcaatgcat cactcaatat tgcaagcac 2400
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tccggagcta ccagttaggg atcgccaggg accacttctt gactaaggag 2550
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cgtgaattaa aaacgccacc ttgggctcga gcagcgacc gaaccagccc 2650
cgtgccagcc cgggtccccag acccaagcct gaccccatcc gagtggaatt 2700
tgagtcctaa agaataaaaa gagtcgatgc atgaaaaaaaa aaaaaaaaaa 2750
aaaaaaaaaa aaaaaaaaaa aa 2772

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<210> SEQ ID NO 57

<211> LENGTH: 419

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 57

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Met Thr Thr Ala Pro Gln Glu Pro Pro Ala Arg Pro Leu Gln Ala
 1                    5                    10
Gly Ser Gly Ala Gly Pro Ala Pro Gly Arg Ala Met Arg Ser Thr
20                    25                    30
Thr Leu Leu Ala Leu Leu Ala Leu Val Leu Leu Tyr Leu Val Ser
35                    40                    45
Gly Ala Leu Val Phe Arg Ala Leu Glu Gln Pro His Glu Gln Gln
50                    55                    60
Ala Gln Arg Glu Leu Gly Glu Val Arg Glu Lys Phe Leu Arg Ala
65                    70                    75
His Pro Cys Val Ser Asp Gln Glu Leu Gly Leu Leu Ile Lys Glu
80                    85                    90
Val Ala Asp Ala Leu Gly Gly Gly Ala Asp Pro Glu Thr Asn Ser
95                    100                   105
Thr Ser Asn Ser Ser His Ser Ala Trp Asp Leu Gly Ser Ala Phe
110                   115                   120
Phe Phe Ser Gly Thr Ile Ile Thr Thr Ile Gly Tyr Gly Asn Val

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	125		130		135
Ala Leu Arg Thr Asp Ala Gly Arg Leu Phe Cys Ile Phe Tyr Ala					
	140		145		150
Leu Val Gly Ile Pro Leu Phe Gly Ile Leu Leu Ala Gly Val Gly					
	155		160		165
Asp Arg Leu Gly Ser Ser Leu Arg His Gly Ile Gly His Ile Glu					
	170		175		180
Ala Ile Phe Leu Lys Trp His Val Pro Pro Glu Leu Val Arg Val					
	185		190		195
Leu Ser Ala Met Leu Phe Leu Leu Ile Gly Cys Leu Leu Phe Val					
	200		205		210
Leu Thr Pro Thr Phe Val Phe Cys Tyr Met Glu Asp Trp Ser Lys					
	215		220		225
Leu Glu Ala Ile Tyr Phe Val Ile Val Thr Leu Thr Thr Val Gly					
	230		235		240
Phe Gly Asp Tyr Val Ala Gly Ala Asp Pro Arg Gln Asp Ser Pro					
	245		250		255
Ala Tyr Gln Pro Leu Val Trp Phe Trp Ile Leu Leu Gly Leu Ala					
	260		265		270
Tyr Phe Ala Ser Val Leu Thr Thr Ile Gly Asn Trp Leu Arg Val					
	275		280		285
Val Ser Arg Arg Thr Arg Ala Glu Met Gly Gly Leu Thr Ala Gln					
	290		295		300
Ala Ala Ser Trp Thr Gly Thr Val Thr Ala Arg Val Thr Gln Arg					
	305		310		315
Ala Gly Pro Ala Ala Pro Pro Pro Glu Lys Glu Gln Pro Leu Leu					
	320		325		330
Pro Pro Pro Pro Cys Pro Ala Gln Pro Leu Gly Arg Pro Arg Ser					
	335		340		345
Pro Ser Pro Pro Glu Lys Ala Gln Leu Pro Ser Pro Pro Thr Ala					
	350		355		360
Ser Ala Leu Asp Tyr Pro Ser Glu Asn Leu Ala Phe Ile Asp Glu					
	365		370		375
Ser Ser Asp Thr Gln Ser Glu Arg Gly Cys Pro Leu Pro Arg Ala					
	380		385		390
Pro Arg Gly Arg Arg Pro Asn Pro Pro Arg Lys Pro Val Arg					
	395		400		405
Pro Arg Gly Pro Gly Arg Pro Arg Asp Lys Gly Val Pro Val					
	410		415		

<210> SEQ ID NO 58

<211> LENGTH: 2814

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 58

```

gccaacactg gccaaacaga agcctccggt cggcctgcag tgcccaagtc           50
ccatggcgag ggcagccoga gtggccgtcg cggctgtagg tccgcatgcc           100
gggcaccgca ccaggcgtct agcagatgga cacaggaaga tccagaagct           150
agtggcaca ctagcaacag agccagatca gaaccagat gctaaactcc           200
tggtggactg cagaggagag ggattcagtc ttctcctgat gtcgattgcg           250
atttctgctg ggagctcaag acgggcgagc tgcccgagat ctcttcgaga           300

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taccccaggg gaggaggaga tgggcaggat ttagtaggac aactcggtta	350
ctaatactt ggcggctggc tgcgaccccc cgggaaatca ggtgcaagca	400
tgtttgectg taggtacctg agttgacacc gaaggtgcct aaagatgctg	450
agcggcgctt ggttcctcag tgtgttaacc gtggccggga tcttacagac	500
agagagtcgc aaaactgcc aagacatttg caagatccgc tgtctgtgcg	550
aagaaaagga aaacgtactg aatatcaact gtgagaacaa aggatttaca	600
acagttagcc tgctccagcc cccccagtat cgaatctatc agctttttct	650
caatggaaac ctcttgacaa gactgtatcc aaacgaattt gtcaattact	700
ccaacgcggg gactcttcac ctaggtaaca acgggttaca ggagatccga	750
acgggggcat tcagtggcct gaaaactctc aaaagactgc atctcaacaa	800
caacaagctt gagatattga gggaggacac cttcctaggc ctggagagcc	850
tggagtatct ccaggccgac tacaattaca tcagtgccat cgaggctggg	900
gcattcagca aacttaacaa gctcaaagtg ctcatcctga atgacaacct	950
tctgctttca ctgcccagca atgtgttccg ctttgcctg ctgaccact	1000
tagacctcag ggggaatagg ctaaaagtaa tgccttttgc tggcgtcctt	1050
gaacatattg gagggatcat ggagattcag ctggagggaa atccatggaa	1100
ttgcacttgt gacttacttc ctctcaaggc ctggctagac accataactg	1150
ttttgtggg agagattgtc tgtgagactc cctttaggtt gcatgggaaa	1200
gacgtgaccc agctgaccag gcaagacctc tgtcccagaa aaagtgccag	1250
tgattccagt cagaggggca gccatgctga caccacgctc caaaggctgt	1300
cacctacaat gaatcctgct ctcaacccaa ccagggtcc gaaagccagc	1350
cggccgcca aatgagaaa tcgtccaact ccccagtgta ctgtgtcaaa	1400
ggacaggcaa agttttggac ccatcatggt gtaccagacc aagtctcctg	1450
tgcctctcac ctgtcccagc agctgtgtct gcacctctca gagctcagac	1500
aatggtctga atgtaactg ccaagaaagg aagttcacta atatctctga	1550
cctgcagccc aaaccgacca gtccaagaa actctaccta acagggaact	1600
atcttcaaac tgtctataag aatgacctct tagaatacag ttctttggac	1650
ttactgcact taggaaacaa caggattgca gtcattcagg aaggtgcctt	1700
tacaaactg accagtttac gcagacttta tctgaatggc aattaccttg	1750
aagtgcgtga cccttctatg tttgatggac tgcagagctt gcaatatctc	1800
tatttagagt ataatgtcat taaggaaatt aagcctctga cctttgatgc	1850
tttgattaac ctacagctac tgtttctgaa caacaacctt ctteggctct	1900
tacctgataa tatatttggg gggacggccc taaccaggct gaactgaga	1950
aacaaccatt tttctcaoct gcccgtagaa ggggttctgg atcagctccc	2000
ggctttcatc cagatagatc tgcaggagaa cccctgggac tgtacctgtg	2050
acatcatggg gctgaaagac tggacagAAC atgccaattc ccctgctatc	2100
attaatgagg tgacttgca atctcctgct aagcatgcag gggagatact	2150
aaaatttctg gggaggagg ctatctgtcc agacagccca aacttgcag	2200
atggaacctg cttgtcaatg aatcacaata cagacacacc tcggtgcctt	2250
agtgtgtctc ctagtctcta tctgaaacta cacactgaag ttccactgtc	2300

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tgtcttaatt ctgggattgc ttgttgtttt catcttatct gtctgttttg	2350
gggctggttt attcgtcttt gtcttgaaac gccgaaaggg agtgccgagc	2400
gttcccagga ataccaacaa cttagacgta agctcctttc aattacagta	2450
tgggtcttac aacctgaga ctcaegataa aacagacggc catgtctaca	2500
actatatccc cccacctgtg ggtcagatgt gccaaaaccc catctacatg	2550
cagaaggaag gagaccagt agcctattac cgaaacctgc aggagttcaa	2600
gaccagccta gagaacatat ggagacctg tcttcacaaa aaataaaaaa	2650
gtcagccaag cgtgggtggg tgtgcctgta gttacttagg aggctgaggg	2700
aggacgatcg cttaaagcca ggagtttgag gctgtggtga gctacaattg	2750
cgccactgca cgccagcctg gctacagaac gagacctgc ctctctaaaa	2800
aaaaaaaaaa aaaa	2814

<210> SEQ ID NO 59

<211> LENGTH: 733

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 59

Met	Leu	Ser	Gly	Val	Trp	Phe	Leu	Ser	Val	Leu	Thr	Val	Ala	Gly	1	5	10	15
Ile	Leu	Gln	Thr	Glu	Ser	Arg	Lys	Thr	Ala	Lys	Asp	Ile	Cys	Lys	20	25	30	
Ile	Arg	Cys	Leu	Cys	Glu	Glu	Lys	Glu	Asn	Val	Leu	Asn	Ile	Asn	35	40	45	
Cys	Glu	Asn	Lys	Gly	Phe	Thr	Thr	Val	Ser	Leu	Leu	Gln	Pro	Pro	50	55	60	
Gln	Tyr	Arg	Ile	Tyr	Gln	Leu	Phe	Leu	Asn	Gly	Asn	Leu	Leu	Thr	65	70	75	
Arg	Leu	Tyr	Pro	Asn	Glu	Phe	Val	Asn	Tyr	Ser	Asn	Ala	Val	Thr	80	85	90	
Leu	His	Leu	Gly	Asn	Asn	Gly	Leu	Gln	Glu	Ile	Arg	Thr	Gly	Ala	95	100	105	
Phe	Ser	Gly	Leu	Lys	Thr	Leu	Lys	Arg	Leu	His	Leu	Asn	Asn	Asn	110	115	120	
Lys	Leu	Glu	Ile	Leu	Arg	Glu	Asp	Thr	Phe	Leu	Gly	Leu	Glu	Ser	125	130	135	
Leu	Glu	Tyr	Leu	Gln	Ala	Asp	Tyr	Asn	Tyr	Ile	Ser	Ala	Ile	Glu	140	145	150	
Ala	Gly	Ala	Phe	Ser	Lys	Leu	Asn	Lys	Leu	Lys	Val	Leu	Ile	Leu	155	160	165	
Asn	Asp	Asn	Leu	Leu	Leu	Ser	Leu	Pro	Ser	Asn	Val	Phe	Arg	Phe	170	175	180	
Val	Leu	Leu	Thr	His	Leu	Asp	Leu	Arg	Gly	Asn	Arg	Leu	Lys	Val	185	190	195	
Met	Pro	Phe	Ala	Gly	Val	Leu	Glu	His	Ile	Gly	Gly	Ile	Met	Glu	200	205	210	
Ile	Gln	Leu	Glu	Glu	Asn	Pro	Trp	Asn	Cys	Thr	Cys	Asp	Leu	Leu	215	220	225	
Pro	Leu	Lys	Ala	Trp	Leu	Asp	Thr	Ile	Thr	Val	Phe	Val	Gly	Glu	230	235	240	

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Ile	Val	Cys	Glu	Thr	Pro	Phe	Arg	Leu	His	Gly	Lys	Asp	Val	Thr	245	250	255
Gln	Leu	Thr	Arg	Gln	Asp	Leu	Cys	Pro	Arg	Lys	Ser	Ala	Ser	Asp	260	265	270
Ser	Ser	Gln	Arg	Gly	Ser	His	Ala	Asp	Thr	His	Val	Gln	Arg	Leu	275	280	285
Ser	Pro	Thr	Met	Asn	Pro	Ala	Leu	Asn	Pro	Thr	Arg	Ala	Pro	Lys	290	295	300
Ala	Ser	Arg	Pro	Pro	Lys	Met	Arg	Asn	Arg	Pro	Thr	Pro	Arg	Val	305	310	315
Thr	Val	Ser	Lys	Asp	Arg	Gln	Ser	Phe	Gly	Pro	Ile	Met	Val	Tyr	320	325	330
Gln	Thr	Lys	Ser	Pro	Val	Pro	Leu	Thr	Cys	Pro	Ser	Ser	Cys	Val	335	340	345
Cys	Thr	Ser	Gln	Ser	Ser	Asp	Asn	Gly	Leu	Asn	Val	Asn	Cys	Gln	350	355	360
Glu	Arg	Lys	Phe	Thr	Asn	Ile	Ser	Asp	Leu	Gln	Pro	Lys	Pro	Thr	365	370	375
Ser	Pro	Lys	Lys	Leu	Tyr	Leu	Thr	Gly	Asn	Tyr	Leu	Gln	Thr	Val	380	385	390
Tyr	Lys	Asn	Asp	Leu	Leu	Glu	Tyr	Ser	Ser	Leu	Asp	Leu	Leu	His	395	400	405
Leu	Gly	Asn	Asn	Arg	Ile	Ala	Val	Ile	Gln	Glu	Gly	Ala	Phe	Thr	410	415	420
Asn	Leu	Thr	Ser	Leu	Arg	Arg	Leu	Tyr	Leu	Asn	Gly	Asn	Tyr	Leu	425	430	435
Glu	Val	Leu	Tyr	Pro	Ser	Met	Phe	Asp	Gly	Leu	Gln	Ser	Leu	Gln	440	445	450
Tyr	Leu	Tyr	Leu	Glu	Tyr	Asn	Val	Ile	Lys	Glu	Ile	Lys	Pro	Leu	455	460	465
Thr	Phe	Asp	Ala	Leu	Ile	Asn	Leu	Gln	Leu	Leu	Phe	Leu	Asn	Asn	470	475	480
Asn	Leu	Leu	Arg	Ser	Leu	Pro	Asp	Asn	Ile	Phe	Gly	Gly	Thr	Ala	485	490	495
Leu	Thr	Arg	Leu	Asn	Leu	Arg	Asn	Asn	His	Phe	Ser	His	Leu	Pro	500	505	510
Val	Lys	Gly	Val	Leu	Asp	Gln	Leu	Pro	Ala	Phe	Ile	Gln	Ile	Asp	515	520	525
Leu	Gln	Glu	Asn	Pro	Trp	Asp	Cys	Thr	Cys	Asp	Ile	Met	Gly	Leu	530	535	540
Lys	Asp	Trp	Thr	Glu	His	Ala	Asn	Ser	Pro	Val	Ile	Ile	Asn	Glu	545	550	555
Val	Thr	Cys	Glu	Ser	Pro	Ala	Lys	His	Ala	Gly	Glu	Ile	Leu	Lys	560	565	570
Phe	Leu	Gly	Arg	Glu	Ala	Ile	Cys	Pro	Asp	Ser	Pro	Asn	Leu	Ser	575	580	585
Asp	Gly	Thr	Val	Leu	Ser	Met	Asn	His	Asn	Thr	Asp	Thr	Pro	Arg	590	595	600
Ser	Leu	Ser	Val	Ser	Pro	Ser	Ser	Tyr	Pro	Glu	Leu	His	Thr	Glu	605	610	615
Val	Pro	Leu	Ser	Val	Leu	Ile	Leu	Gly	Leu	Leu	Val	Val	Phe	Ile	620	625	630
Leu	Ser	Val	Cys	Phe	Gly	Ala	Gly	Leu	Phe	Val	Phe	Val	Leu	Lys			

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635		640		645										
Arg	Arg	Lys	Gly	Val	Pro	Ser	Val	Pro	Arg	Asn	Thr	Asn	Asn	Leu
				650					655					660
Asp	Val	Ser	Ser	Phe	Gln	Leu	Gln	Tyr	Gly	Ser	Tyr	Asn	Thr	Glu
				665					670					675
Thr	His	Asp	Lys	Thr	Asp	Gly	His	Val	Tyr	Asn	Tyr	Ile	Pro	Pro
				680					685					690
Pro	Val	Gly	Gln	Met	Cys	Gln	Asn	Pro	Ile	Tyr	Met	Gln	Lys	Glu
				695					700					705
Gly	Asp	Pro	Val	Ala	Tyr	Tyr	Arg	Asn	Leu	Gln	Glu	Phe	Lys	Thr
				710					715					720
Ser	Leu	Glu	Asn	Ile	Trp	Arg	Pro	Cys	Leu	His	Lys	Lys		
				725					730					

<210> SEQ ID NO 60

<211> LENGTH: 3679

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 60

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aaggaggctg ggaggaaaga ggtaagaaag gttagagaac ctacctcaca      50
tctctctggg ctcagaagga ctctgaagat aacaataatt tcagcccatc      100
cactctcctt ccctcccaaa cacacatgtg catgtacaca cacacatata      150
cacacataca ccttcctctc cttcaactgaa gactcacagt cactcaactt      200
gtgagcaggt catagaaaag gacactaaag ccttaaggac aggcctggcc      250
attacctctg cagctccttt ggcttggtga gtcaaaaaac atgggagggg      300
ccaggcacgg tgactcacac ctgtaatccc agcattttgg gagaccgagg      350
tgagcagatc acttgaggtc aggagttcga gaccagcctg gccaacatgg      400
agaaaccccc atctctacta aaaatacaaa aattagccag gagtgggtggc      450
aggtgcctgt aatcccagct actcaggtgg ctgagccagg agaatcgctt      500
gaatccagga ggcggaggat gcagtcagct gagtgcaccg ctgcaactcca      550
gcctgggtga cagaatgaga ctctgtctca aacaacaaa cacgggagga      600
ggggtagata ctgcttctct gcaacctcct taactctgca tcctcttctt      650
ccagggctgc ccctgatggg gcctggcaat gactgagcag gccagcccc      700
agaggacaag gaagagaagg catattgagg agggcaagaa gtgacgcccc      750
gtgtagaatg actgccttgg gaggggtggt ccttgggccc tggcagggtt      800
gctgaccctt accctgcaaa acacaaagag caggactcca gactctcctt      850
gtgaatggtc ccctgccttg cagctccacc atgaggcttc tcgtggcccc      900
actcttgcta gcttgggtgg ctgggtgccac tgccactgtg cccgtggtac      950
cctggcatgt tcctgcccc cctcagtggt cctgcccagat ccggccctgg      1000
tatacgcccc gctcgtccta ccgagaggct accactgtgg actgcaatga      1050
cctattcttg acggcagttc ccccggaact ccccgaggc acacagacct      1100
tgctcctgca gagcaacagc attgtccgtg tggaccagag tgagctgggc      1150
tacctggcca atctcacaga gctggacctg tcccagaaca gcttttcgga      1200
tgcccagac  tgtgatttcc atgcccctgc ccagctgctg agcctgcacc      1250
tagaggagaa ccagctgacc cggctggagg accacagctt tgcagggctg      1300

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gccagcctac aggaactota tctcaaccac aaccagctct accgcatcgc	1350
ccccagggcc tttctggcc tcagcaactt gctgcggctg cacctcaact	1400
ccaacctcct gagggccatt gacagccgct ggtttgaat gctgccaac	1450
ttggagatac tcatgattgg cggcaacaag gtagatgcca tctggacat	1500
gaacttccgg cccctggcca acctgcgtag cctgggtgcta gcaggcatga	1550
acctgcggga gatctccgac tatgcctgg aggggtgca aagcctggag	1600
agcctctcct tctatgacaa ccagctggcc cgggtgcccc ggccggcact	1650
ggaacaggtg cccgggctca agttcctaga cctcaacaag aaccgctcc	1700
agcgggtagg gccgggggac tttgccaaca tgctgcacct taaggagctg	1750
ggactgaaca acatggagga gctgggtctcc atcgacaagt ttgccctggt	1800
gaacctcccc gagctgacca agctggacat caccaataac ccacggctgt	1850
ccttcatcca cccccgccc ttcaccacc tgccccagat ggagacctc	1900
atgctcaaca acaacgctct cagtgccttg caccagcaga cggtaggagtc	1950
cctgccaac ctgcaggagg taggtctcca cggcaacccc atccgctgtg	2000
actgtgcat ccgctgggcc aatgccacgg gcaccctgt ccgcttcac	2050
gagccgcaat ccacctgtg tgcggagcct ccggacctcc agcgcctccc	2100
ggtccgtgag gtgcccttcc gggagatgac ggaccactgt ttgccctca	2150
tctccccacg aagcttcccc ccaagcctcc aggtagccag tggagagagc	2200
atggtgctgc attgccgggc actggccgaa cccgaacccg agatctactg	2250
ggtcactcca gctgggcttc gactgacacc tgcccatgca ggcaggaggt	2300
accgggtgta ccccgagggg acctggagc tgcggagggg gacagcagaa	2350
gaggcagggc tatacacctg tgtggcccag aacctgggtg gggctgacac	2400
taagacgggt agtgtggttg tggccctgct tctcctccag ccaggcaggg	2450
acgaaggaca ggggctggag ctccgggtgc aggagaccca cccctatcac	2500
atcctgctat cttgggtcac cccacccaac acagtgtcca ccaacctcac	2550
ctggtccagt gcctcctccc tccggggcca gggggccaca gctctggccc	2600
gcctgcctcg gggaaacccac agctacaaca ttaccgcct ccttcaggcc	2650
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gttgcttgt gtatgggcca ggaccaaaga ggccacttct tgccacagag	2750
ccttagggga tegtctggg ctcatgcca tctggctct cgctgtcctt	2800
ctcctggcag ctgggctagc ggcccacctt ggcacaggcc aaccaggaa	2850
gggtgtgggt gggaggcggc ctctccctcc agcctgggct ttctggggct	2900
ggagtgeccc ttctgtccgg gttgtgtctg ctcccctcg cctgccctgg	2950
aatccaggga ggaagctgcc cagatcctca gaaggggaga cactggtgcc	3000
accattgtct caaaattctt gaagctcagc ctgttctcag cagtagagaa	3050
atcactagga ctacttttta ccaaaagaga agcagtctgg gccagatgcc	3100
ctgccaggaa agggacatgg acccacgtgc ttgaggcctg gcagctgggc	3150
caagacagat ggggctttgt ggcctgggg gtgcttctgc agcctgaaa	3200
aagttgcctt tacctcctag ggtcacctct gctgccatc tgaggaacat	3250

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ctccaaggaa caggaggac tttggctaga gcctcctgcc tccccatctt      3300
ctctctgccc agaggctcct gggcctggct tggctgtccc ctacctgtgt      3350
ccccgggtg cacccttcc tcttctcttt ctctgtacag tctcagttgc      3400
ttgctcttgt gcctcctggg caagggtga aggaggccac tccatctcac      3450
ctcggggggc tgcctcaat gtgggagtga cccagccag atctgaagga      3500
catttgggag agggatgccc aggaacgcct catctcagca gcctgggctc      3550
ggcattccga agctgacttt ctataggcaa tttgtacct ttgtggagaa      3600
atgtgtcacc tcccccaacc cgattcactc ttttctctg ttttgtaaaa      3650
aataaaaaata aataataaca ataaaaaaa      3679

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<210> SEQ ID NO 61

<211> LENGTH: 713

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 61

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Met Arg Leu Leu Val Ala Pro Leu Leu Leu Ala Trp Val Ala Gly
  1           5           10           15
Ala Thr Ala Thr Val Pro Val Val Pro Trp His Val Pro Cys Pro
          20           25           30
Pro Gln Cys Ala Cys Gln Ile Arg Pro Trp Tyr Thr Pro Arg Ser
          35           40           45
Ser Tyr Arg Glu Ala Thr Thr Val Asp Cys Asn Asp Leu Phe Leu
          50           55           60
Thr Ala Val Pro Pro Ala Leu Pro Ala Gly Thr Gln Thr Leu Leu
          65           70           75
Leu Gln Ser Asn Ser Ile Val Arg Val Asp Gln Ser Glu Leu Gly
          80           85           90
Tyr Leu Ala Asn Leu Thr Glu Leu Asp Leu Ser Gln Asn Ser Phe
          95          100          105
Ser Asp Ala Arg Asp Cys Asp Phe His Ala Leu Pro Gln Leu Leu
          110          115          120
Ser Leu His Leu Glu Glu Asn Gln Leu Thr Arg Leu Glu Asp His
          125          130          135
Ser Phe Ala Gly Leu Ala Ser Leu Gln Glu Leu Tyr Leu Asn His
          140          145          150
Asn Gln Leu Tyr Arg Ile Ala Pro Arg Ala Phe Ser Gly Leu Ser
          155          160          165
Asn Leu Leu Arg Leu His Leu Asn Ser Asn Leu Leu Arg Ala Ile
          170          175          180
Asp Ser Arg Trp Phe Glu Met Leu Pro Asn Leu Glu Ile Leu Met
          185          190          195
Ile Gly Gly Asn Lys Val Asp Ala Ile Leu Asp Met Asn Phe Arg
          200          205          210
Pro Leu Ala Asn Leu Arg Ser Leu Val Leu Ala Gly Met Asn Leu
          215          220          225
Arg Glu Ile Ser Asp Tyr Ala Leu Glu Gly Leu Gln Ser Leu Glu
          230          235          240
Ser Leu Ser Phe Tyr Asp Asn Gln Leu Ala Arg Val Pro Arg Arg
          245          250          255
Ala Leu Glu Gln Val Pro Gly Leu Lys Phe Leu Asp Leu Asn Lys
          260          265          270

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Asn	Pro	Leu	Gln	Arg	Val	Gly	Pro	Gly	Asp	Phe	Ala	Asn	Met	Leu	275	280	285
His	Leu	Lys	Glu	Leu	Gly	Leu	Asn	Asn	Met	Glu	Glu	Leu	Val	Ser	290	295	300
Ile	Asp	Lys	Phe	Ala	Leu	Val	Asn	Leu	Pro	Glu	Leu	Thr	Lys	Leu	305	310	315
Asp	Ile	Thr	Asn	Asn	Pro	Arg	Leu	Ser	Phe	Ile	His	Pro	Arg	Ala	320	325	330
Phe	His	His	Leu	Pro	Gln	Met	Glu	Thr	Leu	Met	Leu	Asn	Asn	Asn	335	340	345
Ala	Leu	Ser	Ala	Leu	His	Gln	Gln	Thr	Val	Glu	Ser	Leu	Pro	Asn	350	355	360
Leu	Gln	Glu	Val	Gly	Leu	His	Gly	Asn	Pro	Ile	Arg	Cys	Asp	Cys	365	370	375
Val	Ile	Arg	Trp	Ala	Asn	Ala	Thr	Gly	Thr	Arg	Val	Arg	Phe	Ile	380	385	390
Glu	Pro	Gln	Ser	Thr	Leu	Cys	Ala	Glu	Pro	Pro	Asp	Leu	Gln	Arg	395	400	405
Leu	Pro	Val	Arg	Glu	Val	Pro	Phe	Arg	Glu	Met	Thr	Asp	His	Cys	410	415	420
Leu	Pro	Leu	Ile	Ser	Pro	Arg	Ser	Phe	Pro	Pro	Ser	Leu	Gln	Val	425	430	435
Ala	Ser	Gly	Glu	Ser	Met	Val	Leu	His	Cys	Arg	Ala	Leu	Ala	Glu	440	445	450
Pro	Glu	Pro	Glu	Ile	Tyr	Trp	Val	Thr	Pro	Ala	Gly	Leu	Arg	Leu	455	460	465
Thr	Pro	Ala	His	Ala	Gly	Arg	Arg	Tyr	Arg	Val	Tyr	Pro	Glu	Gly	470	475	480
Thr	Leu	Glu	Leu	Arg	Arg	Val	Thr	Ala	Glu	Glu	Ala	Gly	Leu	Tyr	485	490	495
Thr	Cys	Val	Ala	Gln	Asn	Leu	Val	Gly	Ala	Asp	Thr	Lys	Thr	Val	500	505	510
Ser	Val	Val	Val	Gly	Arg	Ala	Leu	Leu	Gln	Pro	Gly	Arg	Asp	Glu	515	520	525
Gly	Gln	Gly	Leu	Glu	Leu	Arg	Val	Gln	Glu	Thr	His	Pro	Tyr	His	530	535	540
Ile	Leu	Leu	Ser	Trp	Val	Thr	Pro	Pro	Asn	Thr	Val	Ser	Thr	Asn	545	550	555
Leu	Thr	Trp	Ser	Ser	Ala	Ser	Ser	Leu	Arg	Gly	Gln	Gly	Ala	Thr	560	565	570
Ala	Leu	Ala	Arg	Leu	Pro	Arg	Gly	Thr	His	Ser	Tyr	Asn	Ile	Thr	575	580	585
Arg	Leu	Leu	Gln	Ala	Thr	Glu	Tyr	Trp	Ala	Cys	Leu	Gln	Val	Ala	590	595	600
Phe	Ala	Asp	Ala	His	Thr	Gln	Leu	Ala	Cys	Val	Trp	Ala	Arg	Thr	605	610	615
Lys	Glu	Ala	Thr	Ser	Cys	His	Arg	Ala	Leu	Gly	Asp	Arg	Pro	Gly	620	625	630
Leu	Ile	Ala	Ile	Leu	Ala	Leu	Ala	Val	Leu	Leu	Leu	Ala	Ala	Gly	635	640	645
Leu	Ala	Ala	His	Leu	Gly	Thr	Gly	Gln	Pro	Arg	Lys	Gly	Val	Gly	650	655	660

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Gly Arg Arg Pro Leu Pro Pro Ala Trp Ala Phe Trp Gly Trp Ser
665 670 675

Ala Pro Ser Val Arg Val Val Ser Ala Pro Leu Val Leu Pro Trp
680 685 690

Asn Pro Gly Arg Lys Leu Pro Arg Ser Ser Glu Gly Glu Thr Leu
695 700 705

Leu Pro Pro Leu Ser Gln Asn Ser
710

<210> SEQ ID NO 62
<211> LENGTH: 1186
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: Unsure
<222> LOCATION: 54-55
<223> OTHER INFORMATION: Unknown base

<400> SEQUENCE: 62

```

ggcacgagcc ggcaagccga gctaggggtga aaactggggg cgcaccagga      50
tgtningacag aaaagcagaa gatgagactc tgttcattca cttttcctag      100
gcccatectg tggatcatct tccccctccc atcatacctc ctcttctctg      150
gagcctctgc cggcttggct gtaatgggtg cacttacctg gatatttcag      200
tgggaggatg aaaggcgaga ctcacctac gcggtgggac agatggggag      250
aggaaaaagg cagagatggc caggagaggg gtgcaggaca aaccagagag      300
gttgggtcag gggaaaaggg tggggagaaa gaggggtgca ggccctgcag      350
gccggttagc cagcagctgc ggccctcccg ggcccttggc atccaacttc      400
gcagacaggg taccagctc ctgggtgtgta tcataggatt tgttcacata      450
gtgttatgca tgatctctgt aaggttaaga agccgtgggtg gtgcaccatg      500
acatccaacc cgtatatata aagataaata tatatatata tgatgtaaa      550
ttatggcaag agaaattata gcaactgaggg cctctctgcc ctgctggacc      600
aagcaaaact aagccttttg gtttgggtat tatgtttcgt tttgttattt      650
gtttgttttt gtggcttgtc ttatgtctgt atagcacaag tgccagtcgg      700
attgtctctg attacagaat agtgttttta attcatcaat gttctagtta      750
atgtctacct cagcacctcc tcttagocta attttaggag gttgccaat      800
tttgtttctt caattttact ggttactttt ttgtacaaat caatctcttt      850
ctctctttct ctctctccc cctctcacc ttgcccctct catctccctc      900
tcccgccctc ccctcctccc tctggctccc cgtctcattt ctgtccactc      950
cattctctct ccctctctcc tgccctctgc tgccccctcc ccagcccact     1000
tccccgagtt gtgcttgccg ctctctatct gttctagttc cgaagcagtt     1050
tcaactgaag ttgtgcagtc ctggttgca gctttccgat ctgcctctgt     1100
ttcgtgtaga ttgacgcggt tctttgtaat ttcagtgttt ctgacaagat     1150
ttaaaaaaaaa aaaaggaaa aaaaaaaaaa aaaaaa      1186

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<210> SEQ ID NO 63
<211> LENGTH: 145
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 63

-continued

Met	Ser	Thr	Ser	Ala	Pro	Pro	Leu	Ser	Leu	Ile	Leu	Gly	Gly	Cys
1				5					10					15
Pro	Ile	Leu	Phe	Leu	Gln	Phe	Tyr	Trp	Leu	Leu	Phe	Cys	Thr	Asn
				20					25					30
Gln	Ser	Leu	Ser	Leu	Phe	Leu	Ser	Ser	Pro	Pro	Leu	Thr	Leu	Ala
				35					40					45
Leu	Ser	Ile	Ser	Leu	Ser	Arg	Pro	Pro	Leu	Leu	Pro	Leu	Ala	Pro
				50					55					60
Arg	Leu	Ile	Ser	Val	His	Ser	Ile	Leu	Ser	Pro	Ser	Leu	Leu	Pro
				65					70					75
Pro	Ala	Ala	Pro	Ser	Pro	Ala	His	Phe	Pro	Glu	Leu	Cys	Leu	Pro
				80					85					90
Leu	Leu	Ile	Cys	Ser	Ser	Ser	Glu	Ala	Val	Ser	Leu	Glu	Val	Val
				95					100					105
Gln	Ser	Trp	Leu	Gln	Leu	Ser	Ala	Ser	Ala	Phe	Val	Ser	Cys	Arg
				110					115					120
Leu	Thr	Arg	Phe	Phe	Val	Ile	Ser	Val	Phe	Leu	Thr	Arg	Phe	Lys
				125					130					135
Lys	Lys	Lys	Arg	Lys	Lys	Lys	Lys	Lys	Lys					
				140					145					

<210> SEQ ID NO 64

<211> LENGTH: 1685

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 64

```

ccccacgctc cgcacctcgg ccccgggctc cgaagcggct cgggggcgcc          50
ctttcggtea acatcgtagt cccccccctc cccatcccca gccccggggg          100
attcaggctc gccagcgccc agccaggggag cgggcccggga agcgcgatgg          150
gggccccagc gcctcgcctc ctgctcctgc tcctgctgtt cgctgctgctc          200
tgggcgcgccg gcggggccaa cctctcccag gacgacagcc agccctggac          250
atctgatgaa acagtgggtg ctggtggcac cgtggtgctc aagtgccaaag          300
tgaaagatca cgaggactca tcctgcaat ggtctaacct tgctcagcag          350
actctctact ttggggagaa gagagccctt cgagataatc gaattcagct          400
ggttacctct acgccccacg agctcagcat cagcatcagc aatgtggccc          450
tggcagacga gggcgagtac acctgctcaa tcttcactat gcctgtgcga          500
actgccaagt cctcctgcac tgtgctagga attccacaga agcccatcat          550
cactggttat aaatcttcat tacgggaaaa agacacagcc accctaaact          600
gtcagtcttc tgggagcaag cctgcagccc ggctcacctg gagaaagggt          650
gaccaagaac tccacggaga accaacccgc atacaggaag atcccaatgg          700
taaaaccttc actgtcagca gctcgggtgac attccaggtt acccgggagg          750
atgatggggc gagcatcgtg tgctctgtga accatgaatc tctaaaggga          800
gctgacagat ccacctctca acgcattgaa gttttataca caccaactgc          850
gatgattagg ccagaccctc cccatcctcg tgagggccag aagctgtgtc          900
tacactgtga gggtcgcggc aatccagtcc cccagcagta cctatggggag          950
aaggagggca gtgtgccacc cctgaagatg acccaggaga gtgccctgat          1000

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cttcccttct ctcaacaaga gtgacagtgg cacctacggc tgcacagcca      1050
ccagcaacat gggcagctac aaggcctact acacctcaa tgттаатgac      1100
cccagtcegg tgcctctctc ctccagcacc taccagcca tcatcggtgg      1150
gatcgtggct ttcattgtct tctgtctgct catcatgctc atcttccttg      1200
gccactactt gatccggcac aaaggaacct acctgacaca tgaggcaaaa      1250
ggctccgacg atgtccaga cgcggacacg gccatcatca atgcagaagg      1300
cgggcagtca ggaggggacg acaagaagga atatttcac tagaggcgcc      1350
tgcccacttc ctgcgcccc caggggccct gtggggactg ctggggcctg      1400
caccaaccgg gacttgtaga gagcaaccgc agggccgccc ctcccgttg      1450
ctccccagcc caccacccc cctgtacaga atgtctgctt tgggtgctgt      1500
tttgactcog gtttggaatg gggaggagg agggcggggg gaggggagg      1550
ttgcctcag ccctttccgt ggcttctctg catttgggtt attattatt      1600
ttgtaacaat cccaaatcaa atctgtctcc aggctggaga ggcaggagcc      1650
ctggggtgag aaaagcaaaa aacaaacaaa aaaca      1685

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<210> SEQ ID NO 65

<211> LENGTH: 398

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 65

```

Met Gly Ala Pro Ala Ala Ser Leu Leu Leu Leu Leu Leu Phe
 1                5                10                15
Ala Cys Cys Trp Ala Pro Gly Gly Ala Asn Leu Ser Gln Asp Asp
 20                25
Ser Gln Pro Trp Thr Ser Asp Glu Thr Val Val Ala Gly Gly Thr
 35                40                45
Val Val Leu Lys Cys Gln Val Lys Asp His Glu Asp Ser Ser Leu
 50                55                60
Gln Trp Ser Asn Pro Ala Gln Gln Thr Leu Tyr Phe Gly Glu Lys
 65                70                75
Arg Ala Leu Arg Asp Asn Arg Ile Gln Leu Val Thr Ser Thr Pro
 80                85                90
His Glu Leu Ser Ile Ser Ile Ser Asn Val Ala Leu Ala Asp Glu
 95                100               105
Gly Glu Tyr Thr Cys Ser Ile Phe Thr Met Pro Val Arg Thr Ala
110                115                120
Lys Ser Leu Val Thr Val Leu Gly Ile Pro Gln Lys Pro Ile Ile
125                130                135
Thr Gly Tyr Lys Ser Ser Leu Arg Glu Lys Asp Thr Ala Thr Leu
140                145                150
Asn Cys Gln Ser Ser Gly Ser Lys Pro Ala Ala Arg Leu Thr Trp
155                160                165
Arg Lys Gly Asp Gln Glu Leu His Gly Glu Pro Thr Arg Ile Gln
170                175                180
Glu Asp Pro Asn Gly Lys Thr Phe Thr Val Ser Ser Ser Val Thr
185                190                195
Phe Gln Val Thr Arg Glu Asp Asp Gly Ala Ser Ile Val Cys Ser
200                205                210
Val Asn His Glu Ser Leu Lys Gly Ala Asp Arg Ser Thr Ser Gln

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	215		220		225
Arg Ile Glu Val Leu Tyr Thr Pro Thr Ala Met Ile Arg Pro Asp					
	230		235		240
Pro Pro His Pro Arg Glu Gly Gln Lys Leu Leu Leu His Cys Glu					
	245		250		255
Gly Arg Gly Asn Pro Val Pro Gln Gln Tyr Leu Trp Glu Lys Glu					
	260		265		270
Gly Ser Val Pro Pro Leu Lys Met Thr Gln Glu Ser Ala Leu Ile					
	275		280		285
Phe Pro Phe Leu Asn Lys Ser Asp Ser Gly Thr Tyr Gly Cys Thr					
	290		295		300
Ala Thr Ser Asn Met Gly Ser Tyr Lys Ala Tyr Tyr Thr Leu Asn					
	305		310		315
Val Asn Asp Pro Ser Pro Val Pro Ser Ser Ser Ser Thr Tyr His					
	320		325		330
Ala Ile Ile Gly Gly Ile Val Ala Phe Ile Val Phe Leu Leu Leu					
	335		340		345
Ile Met Leu Ile Phe Leu Gly His Tyr Leu Ile Arg His Lys Gly					
	350		355		360
Thr Tyr Leu Thr His Glu Ala Lys Gly Ser Asp Asp Ala Pro Asp					
	365		370		375
Ala Asp Thr Ala Ile Ile Asn Ala Glu Gly Gly Gln Ser Gly Gly					
	380		385		390
Asp Asp Lys Lys Glu Tyr Phe Ile					
	395				

<210> SEQ ID NO 66
 <211> LENGTH: 681
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 66

```

cttgatctg cctgccaggc catcctgggc gctgcaggaa gcaacatgac          50
ttaggtaact gcccagaggt gcaccagaca tgatgcagca gccgcgagtg          100
gagacagata ccacgagggc tggcgagggg ccacagcagg cagtgcctgg          150
tcagcctggg tcacgaggca tggctgggtg cgctggtggg tgagccacat          200
gccccgagc tggatccagt ggtggagcac ctcgaactgg cggcaaccgc          250
tgcagcgect gctgtggggt ctggagggga tactctacct gctgctggca          300
ctgatgttgt gccatgcact cttcaccact ggctcccacc tgetgagctc          350
cttgtggcct gtcgtggccg cgggtgtggcg ccacctgcta ccggtctccc          400
tgetgctggt getcagtget ctgcctgccc tcctcttcac ggctccttc          450
ctgetgctct tctccacact getgagcett gtgggectcc tcacctccat          500
gactcaccca ggcgacactc aggatttga tcaatagaag ggcaacccca          550
tcccactgcc tgtgtttggt gagccctggc ctagggcctg agaccccacg          600
gggagagggg gggcaatggg atcagggtc cctgccttgg cagggccacg          650
accctagtc cctaacaggt aggctggcct g          681
    
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<210> SEQ ID NO 67
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

-continued

<400> SEQUENCE: 67

Met Pro Pro Ser Trp Ile Gln Trp Trp Ser Thr Ser Asn Trp Arg
 1 5 10 15
 Gln Pro Leu Gln Arg Leu Leu Trp Gly Leu Glu Gly Ile Leu Tyr
 20 25 30
 Leu Leu Leu Ala Leu Met Leu Cys His Ala Leu Phe Thr Thr Gly
 35 40 45
 Ser His Leu Leu Ser Ser Leu Trp Pro Val Val Ala Ala Val Trp
 50 55 60
 Arg His Leu Leu Pro Ala Leu Leu Leu Leu Val Leu Ser Ala Leu
 65 70 75
 Pro Ala Leu Leu Phe Thr Ala Ser Phe Leu Leu Leu Phe Ser Thr
 80 85 90
 Leu Leu Ser Leu Val Gly Leu Leu Thr Ser Met Thr His Pro Gly
 95 100 105
 Asp Thr Gln Asp Leu Asp Gln
 110

<210> SEQ ID NO 68

<211> LENGTH: 2600

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 68

acatgcgccc tgacagccca acaatggcgg cccccgcgga gtcgctgagg 50
 aggcggaaga ctgggtactc ggatccggag cctgagtcgc cgccccgcgc 100
 ggggcgtggc cccgcaggct ctccggccca tcttcacacg ggcaccttct 150
 ggctgaccgc gatcgtgctc ctgaaggccc tagccttcgt gtacttcgtg 200
 gcattcctgg tggtttcca tcagaacaag cagctcatcg gtgacagggg 250
 gctgcttccc tgcagagtgt tctgaagga cttccagcag tacttccagg 300
 acaggacaag ctgggaagtc ttcagctaca tgcccaccat cctctggctg 350
 atggactggt cagacatgaa ctccaacctg gacttgcctg ctcttctcgg 400
 actgggcatc tcgtctttcg tactgatcac gggttgccgc aacatgcttc 450
 tcatggctgc cctgtggggc ctctacatgt ccctgggtaa tgtgggcat 500
 gtctggctact ctttcggatg ggagtcocag cttctggaga cgggattcct 550
 ggggatcttc ctgtgccctc tgtggacgct gtcaaggctg ccccagcata 600
 cccccacatc ccggattgtc ctgtggggct tccggtggct gatcttcagg 650
 atcatgcttg gagcaggcct gatcaagatc cggggggacc ggtgctggcg 700
 agacctcacc tgcattgact tccactatga gaccagccg atgcccacatc 750
 ctgtggcata ctacctgcac cactcaccct ggtggttcca tcgcttcgag 800
 acgctcagca accacttcat cgagctcctg gtgcccttct tctcttctct 850
 cggccggcgg gcgtgcatca tccacggggg getgcagatc ctgttccagg 900
 ccgtcctcat cgtcagcggg aacctcagct tcctgaactg gctgactatg 950
 gtgcccagcc tggcctgctt tgatgacgcc accctgggat tcttgttccc 1000
 ctctgggcca ggcagcctga aggaccgagt tctgcagatg cagagggaca 1050
 tccgaggggc ccggcccag cccagattcg gctccgtggt gcggcgtgca 1100

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gccaacgtct cgctggggct cctgctggcc tggctcagcg tgcccgtggt      1150
cctcaacttg ctgagctcca ggcaggtcac gaacacccac ttcaactctc      1200
ttcacatcgt caaacacttac ggggccttcg gaagcatcac caaggagcgg      1250
gcgagggtga tcctgcaggg cacagccagc tccaacgcca gcgccccga      1300
tgccatgtgg gaggactacg agttcaagtg caagccaggt gaccccagca      1350
gacggccctg cctcatctcc cctaccact accgctgga ctggctgatg      1400
tggttcgagg ccttcagac ctacgagcac aacgactgga tcatccact      1450
ggctggcaag ctctggcca ggcagccga ggcctgtcc ctgctggcac      1500
acaacccctt cgcgggcagg cccccccca ggtgggtccg aggagagcac      1550
tacaggtaaa agttcagccg tcctgggggc aggcacgccc cggagggcaa      1600
gtggtgggtg cggaaagagga tcggagccta cttccctccg ctcagcctgg      1650
aggagctgag gccctacttc agggaccgtg ggtggcctct gcccgggccc      1700
ctctagacgt gcaccagaaa taaaggcgaa gaccagccc ctcggcggct      1750
cagcaacggt tgccctccc tgcgccagc ccaagctggg catcgccaag      1800
agagacgtgg agaggagagc ggtgggaccc agccccagc acgggggtcc      1850
agggtggggt ctggtgtcac atactgtgc ggcctcccag ccctgccac      1900
ctggggcccc acatccaggc caaccctgt cccagggccc aggggctctg      1950
atctcccate cateccaccc tcctcccaga ggcccagcct ggggctgtgc      2000
cgcccacagg agttgagaca atggcaatcc tgacacctc ctccactaca      2050
gccctgacca tagaccagc caggtagctc ttggggtctc tagcgtccca      2100
gggctgggtt tctgttccct cttcaatggt gtgttccag ccaggctctg      2150
accctcagag ccaagtcct gtcacgtctg ggcagccaa accctgccc      2200
cacagggacc tggacacgcc cggccaggat gtggggtgg atgggceatt      2250
ttctgtccta tcctcatct cccccccgc cacagcctac acgcatccca      2300
cacatgcagg cacacacagc ctgtgcacac atgtgttctt ggcccggttt      2350
catccccca tgactggtgt ctgtgaggtg cagatggaca cagcgcacac      2400
ccagaccctc caccaggctg tgacctgct gcctctgagg ccttgacaag      2450
gcccctcaat cggaggacag ccggccgtgc acacttcat catcgtcgga      2500
caaacagcgt ctactgcaca tttttcttat tcctattctt gagccatagc      2550
tatggcatat tcttctaata ttctattat accacttacc agcttactcg      2600

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<210> SEQ ID NO 69

<211> LENGTH: 567

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 69

```

Met Arg Pro Asp Ser Pro Thr Met Ala Ala Pro Ala Glu Ser Leu
  1             5             10             15
Arg Arg Arg Lys Thr Gly Tyr Ser Asp Pro Glu Pro Glu Ser Pro
             20             25             30
Pro Ala Pro Gly Arg Gly Pro Ala Gly Ser Pro Ala His Leu His
             35             40             45
Thr Gly Thr Phe Trp Leu Thr Arg Ile Val Leu Leu Lys Ala Leu
             50             55             60

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Ala Phe Val Tyr Phe Val Ala Phe Leu Val Ala Phe His Gln Asn	65	70	75
Lys Gln Leu Ile Gly Asp Arg Gly Leu Leu Pro Cys Arg Val Phe	80	85	90
Leu Lys Asp Phe Gln Gln Tyr Phe Gln Asp Arg Thr Ser Trp Glu	95	100	105
Val Phe Ser Tyr Met Pro Thr Ile Leu Trp Leu Met Asp Trp Ser	110	115	120
Asp Met Asn Ser Asn Leu Asp Leu Leu Ala Leu Leu Gly Leu Gly	125	130	135
Ile Ser Ser Phe Val Leu Ile Thr Gly Cys Ala Asn Met Leu Leu	140	145	150
Met Ala Ala Leu Trp Gly Leu Tyr Met Ser Leu Val Asn Val Gly	155	160	165
His Val Trp Tyr Ser Phe Gly Trp Glu Ser Gln Leu Leu Glu Thr	170	175	180
Gly Phe Leu Gly Ile Phe Leu Cys Pro Leu Trp Thr Leu Ser Arg	185	190	195
Leu Pro Gln His Thr Pro Thr Ser Arg Ile Val Leu Trp Gly Phe	200	205	210
Arg Trp Leu Ile Phe Arg Ile Met Leu Gly Ala Gly Leu Ile Lys	215	220	225
Ile Arg Gly Asp Arg Cys Trp Arg Asp Leu Thr Cys Met Asp Phe	230	235	240
His Tyr Glu Thr Gln Pro Met Pro Asn Pro Val Ala Tyr Tyr Leu	245	250	255
His His Ser Pro Trp Trp Phe His Arg Phe Glu Thr Leu Ser Asn	260	265	270
His Phe Ile Glu Leu Leu Val Pro Phe Phe Leu Phe Leu Gly Arg	275	280	285
Arg Ala Cys Ile Ile His Gly Val Leu Gln Ile Leu Phe Gln Ala	290	295	300
Val Leu Ile Val Ser Gly Asn Leu Ser Phe Leu Asn Trp Leu Thr	305	310	315
Met Val Pro Ser Leu Ala Cys Phe Asp Asp Ala Thr Leu Gly Phe	320	325	330
Leu Phe Pro Ser Gly Pro Gly Ser Leu Lys Asp Arg Val Leu Gln	335	340	345
Met Gln Arg Asp Ile Arg Gly Ala Arg Pro Glu Pro Arg Phe Gly	350	355	360
Ser Val Val Arg Arg Ala Ala Asn Val Ser Leu Gly Val Leu Leu	365	370	375
Ala Trp Leu Ser Val Pro Val Val Leu Asn Leu Leu Ser Ser Arg	380	385	390
Gln Val Met Asn Thr His Phe Asn Ser Leu His Ile Val Asn Thr	395	400	405
Tyr Gly Ala Phe Gly Ser Ile Thr Lys Glu Arg Ala Glu Val Ile	410	415	420
Leu Gln Gly Thr Ala Ser Ser Asn Ala Ser Ala Pro Asp Ala Met	425	430	435
Trp Glu Asp Tyr Glu Phe Lys Cys Lys Pro Gly Asp Pro Ser Arg	440	445	450

-continued

Arg Pro Cys Leu Ile Ser Pro Tyr His Tyr Arg Leu Asp Trp Leu
 455 460

Met Trp Phe Ala Ala Phe Gln Thr Tyr Glu His Asn Asp Trp Ile
 470 475

Ile His Leu Ala Gly Lys Leu Leu Ala Ser Asp Ala Glu Ala Leu
 485 490

Ser Leu Leu Ala His Asn Pro Phe Ala Gly Arg Pro Pro Pro Arg
 500 505

Trp Val Arg Gly Glu His Tyr Arg Tyr Lys Phe Ser Arg Pro Gly
 515 520

Gly Arg His Ala Ala Glu Gly Lys Trp Trp Val Arg Lys Arg Ile
 530 535

Gly Ala Tyr Phe Pro Pro Leu Ser Leu Glu Glu Leu Arg Pro Tyr
 545 550

Phe Arg Asp Arg Gly Trp Pro Leu Pro Gly Pro Leu
 560 565

<210> SEQ ID NO 70
 <211> LENGTH: 1900
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 70

```

ggcacgagga gaagactttg gtggggtagt ctcggggcag ctcagcggcc      50
cgctgtgccc gtttctggcc tcgctcgcag cttgcacgtc gagactcgta      100
ggccgcaccg tagggcgagc gtgcgggctc cgcgccgggc cgcctcgggg      150
tctgggceca gccgcagcct cttctaccgc ggccggttgg gagtgcgcgc      200
gagatgcagc ctccggggccc gccccgggcc tatgccccca ctaacgggga      250
cttcaccttt gtctcctcag cagacgcgga agatctcagt ggttcaatag      300
catccccaga tgtcaaatta aatcctggtg gagattttat caaagaatct      350
acagctacta catttctgag acaaagaggt tatggctggc ttctggaagt      400
tgaagatgat gatcctgaag ataacaagcc actcttgaa gaattggaca      450
ttgatctaaa ggatatttac tacaaaatcc gatgtgtttt gatgccaatg      500
ccatcacttg gttttaatag acaagtggtg agagacaatc ctgacttttg      550
gggtcctctg gctgtgttcc ttttctttc catgatatca ttatatggac      600
agtttagggg ggtctcatgg attataacca ttggatatt tggttcacta      650
acaattttct tactggccag agttcttggg ggagaagttg catatggcca      700
agtccttggg gttataggat attcattact tcctctcatt gtaatagccc      750
ctgtactttt ggtggttgga tcatttgaag tgggtgtctac acttataaaa      800
ctgtttggtg tgttttgggc tgccctacagt gctgcttcat tgtagtggg      850
tgaagaatc aagacaaaa agcctcttct gatttatcca atctttttat      900
tatacattta tttttgtcg ttatatactg gtgtgtgatc caagtatac      950
atgaatagaa aaagatggtg ttaaatttgt gtgtaggctg ggaattcttg      1000
ctgaaggaat tggagaaaac ctgttgctgc aaaattttac atgttccaga      1050
tggaaagggg agtctaagcg ctttttaaaa caattttttt ttgtatttaa      1100
ttaagcaatt gcagttatct gggatttttg ggtcagaatt ttaaattctg      1150
tttgattctc catattccag tgaataaaat acaaaagcat tgtgttttta      1200
    
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agattgtgtc gatattcacc taaaaacttg tgccaaaagc acctggattg      1250
gtaattatat ttcacttaaa gggtaaattt gacaatatct tgataatcaa      1300
aagtgaattt tttttcttca aaatgttttc tccagcatca cagatcctgc      1350
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tatttacagc atcagtaaat atttttaagt ggtacttcta aatcataaaa      1800
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<210> SEQ ID NO 71

<211> LENGTH: 240

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 71

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Ser Ile Ala Ser Pro Asp Val Lys Leu Asn Leu Gly Gly Asp Phe
          35          40          45
Ile Lys Glu Ser Thr Ala Thr Thr Phe Leu Arg Gln Arg Gly Tyr
          50          55          60
Gly Trp Leu Leu Glu Val Glu Asp Asp Asp Pro Glu Asp Asn Lys
          65          70          75
Pro Leu Leu Glu Glu Leu Asp Ile Asp Leu Lys Asp Ile Tyr Tyr
          80          85          90
Lys Ile Arg Cys Val Leu Met Pro Met Pro Ser Leu Gly Phe Asn
          95          100          105
Arg Gln Val Val Arg Asp Asn Pro Asp Phe Trp Gly Pro Leu Ala
          110          115          120
Val Val Leu Phe Phe Ser Met Ile Ser Leu Tyr Gly Gln Phe Arg
          125          130          135
Val Val Ser Trp Ile Ile Thr Ile Trp Ile Phe Gly Ser Leu Thr
          140          145          150
Ile Phe Leu Leu Ala Arg Val Leu Gly Gly Glu Val Ala Tyr Gly
          155          160          165
Gln Val Leu Gly Val Ile Gly Tyr Ser Leu Leu Pro Leu Ile Val
          170          175          180
Ile Ala Pro Val Leu Leu Val Val Gly Ser Phe Glu Val Val Ser
          185          190          195
Thr Leu Ile Lys Leu Phe Gly Val Phe Trp Ala Ala Tyr Ser Ala
          200          205          210

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-continued

Ala Ser Leu Leu Val Gly Glu Glu Phe Lys Thr Lys Lys Pro Leu
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Leu Ile Tyr Pro Ile Phe Leu Leu Tyr Ile Tyr Phe Leu Ser Leu
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<210> SEQ ID NO 72
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<400> SEQUENCE: 74

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<400> SEQUENCE: 75

gtgaggacgg ggcgagac 18

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What is claimed is:

1. A method of inhibiting the growth of a cell that expresses a protein having:

- (a) the amino acid sequence—shown in FIG. 10 (SEQ ID NO: 10), with or without its associated signal peptide;
 (b) an extracellular domain of the polypeptide having the amino acid sequence shown in FIG. 10 (SEQ ID NO: 10), with or without its associated signal peptide;
 (c) a polypeptide encoded by the nucleotide sequence shown in FIG. 9 (SEQ ID NO: 9); or
 (d) a polypeptide encoded by the full-length coding region of the nucleotide sequence shown in FIG. 9 (SEQ ID NO: 9),

said method comprising contacting said cell with an antibody that binds to said protein, wherein said antibody is conjugated to a growth inhibitory agent or cytotoxic agent and is internalized by and inhibits the growth of a cell expressing said polypeptide, wherein said cell is a cancer cell selected from the group consisting of a leukemia cell, a lymphoma cell and a myeloma cell.

2. The method of claim 1, wherein said antibody is a monoclonal antibody.

3. The method of claim 1, wherein said antibody is an antibody fragment.

4. The method of claim 1, wherein said antibody is a chimeric or a humanized antibody.

5. The method of claim 1, wherein said antibody is conjugated to the growth inhibitory agent or cytotoxic agent via a linker.

6. The method of claim 5, wherein the linker is a peptidase-sensitive linker.

7. The method of claim 6, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

8. The method of claim 6, wherein the cytotoxic agent is a toxin.

9. The method of claim 8, wherein the toxin is selected from the group consisting of monomethylauristatin (MMAE), maytansinoid and calicheamicin.

10. The method of claim 8, wherein the toxin is a maytansinoid.

11. The method of claim 1, wherein said antibody is produced in bacteria.

12. The method of claim 1, wherein said antibody is produced in CHO cells.

13. The method of claim 1 wherein said cancer cell is further exposed to radiation treatment or a chemotherapeutic agent.

14. The method of claim 1, wherein said protein is more abundantly expressed by said cancer cell compared to a non-cancer cell.

15. The method of claim 1 which causes the death of said cell.

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16. The method of claim 1, wherein said lymphoma cell is selected from the group consisting of a follicular lymphoma cell, mantle cell lymphoma cell or diffuse large cell lymphoma cell.

17. A method for treating a cell proliferative disorder associated with increased expression or activity of a protein having:

- (a) the amino acid sequence shown in FIG. 10 (SEQ ID NO: 10), with or without its associated signal peptide;
- (b) an extracellular domain of the polypeptide having the amino acid sequence shown in FIG. 10 (SEQ ID NO: 10), with or without its associated signal peptide;
- (c) a polypeptide encoded by the nucleotide sequence shown in FIG. 9 (SEQ ID NO: 9); or
- (d) a polypeptide encoded by the full-length coding region of the nucleotide sequence shown in FIG. 9 (SEQ ID NO: 9),

said method comprising administering to a subject in need of such treatment an effective amount of an antibody of said protein, wherein said antibody is conjugated to a growth inhibitory agent or cytotoxic agent and is internalized by and thereby effectively treating said cell proliferative disorder, wherein said cell proliferative disorder is a cancer selected from the group consisting of leukemia, lymphoma and myeloma.

18. The method of claim 17, wherein said antibody is an anti-TAHO polypeptide antibody.

19. A method for inhibiting the growth of a cell, wherein the growth of said cell is at least in part dependent upon a growth potentiating effect of a protein having:

- (a) the amino acid sequence shown in FIG. 10 (SEQ ID NO: 10), with or without its associated signal peptide;
- (b) an extracellular domain of the polypeptide having the amino acid sequence shown in FIG. 10 (SEQ ID NO: 10), with or without its associated signal peptide;
- (c) a polypeptide encoded by the nucleotide sequence shown in FIG. 9 (SEQ ID NO: 9); or
- (d) a polypeptide encoded by the full-length coding region of the nucleotide sequence shown in FIG. 9 (SEQ ID NO: 9),

said method comprising contacting said protein with an antibody, that binds to said protein, wherein said antibody is conjugated to a growth inhibitory agent or cytotoxic agent and is internalized by and inhibits the growth of a cell expressing said polypeptide, wherein said cell is a cancer cell selected from the group consisting of a leukemia cell, a lymphoma cell and a myeloma cell.

20. The method of claim 19, wherein said protein is expressed by said cell.

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21. The method of claim 19, wherein the binding of said antibody to said protein antagonizes a cell growth-potentiating activity of said protein.

22. The method of claim 19, wherein the binding of said antibody to said protein induces the death of said cell.

23. The method of claim 19, wherein said antibody is a monoclonal antibody.

24. The method of claim 19, wherein said antibody is an antibody fragment.

25. The method of claim 19, wherein said antibody is a chimeric or a humanized antibody.

26. The method of claim 19, wherein said antibody is conjugated to the growth inhibitory agent or cytotoxic agent via a linker.

27. The method of claim 26, wherein said linker is a peptidase-sensitive linker.

28. The method of claim 27, wherein said cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.

29. The method of claim 27, wherein the cytotoxic agent is a toxin.

30. The method of claim 29, wherein the toxin is selected from the group consisting of monomethylauristatin (MMAE), maytansinoid and calicheamicin.

31. The method of claim 29, wherein the toxin is a maytansinoid.

32. The method of claim 19, wherein said antibody is produced in bacteria.

33. The method of claim 19, wherein said antibody is produced in CHO cells.

34. The method of claim 19, wherein said lymphoma cell is selected from the group consisting of a follicular lymphoma cell, mantle cell lymphoma cell or diffuse large cell lymphoma cell.

35. The method of claim 5, wherein the antibody is conjugated to a maytansinoid and wherein the linker is selected from the group consisting of sulfosuccinimidyl maleimidomethyl cyclohexane carboxylate (SMCC) and N-succinimidyl-4-(2-pyridylthio)pentanoate (SPP).

36. The method of claim 35, wherein the linker is SMCC.

37. The method of claim 35, wherein the linker is SPP.

38. The method of claim 6, wherein the antibody is conjugated to a maytansinoid and wherein the peptidase-sensitive linker comprises a valine-citrulline (vc) dipeptide linker reagent having a maleimide component and a paraaminobenzylcarbonyl (PAB) self-immolative component (MC-vc-PAB).

39. The method of claim 5, wherein the antibody is conjugated to monomethylauristatin (MMAE) via vc-PAB.

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